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(54) **NUCLEIC ACIDS ENCODING ANTIBODIES THAT BIND COLONY STIMULATING FACTOR 1 RECEPTOR (CSF1R)**

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(57) **ABSTRACT**

Antibodies that bind CSF1R are provided. Antibody heavy chains and light chains that are capable of forming antibodies that bind CSF1R are also provided. Polynucleotides encoding antibodies to CSF1R are provided. Polynucleotides encoding antibody heavy chains and light chains are also provided. Methods of treatment using antibodies to CSF1R are provided. Such methods include, but are not limited to, methods of treating rheumatoid arthritis, bone loss, and multiple sclerosis.

23 Claims, 16 Drawing Sheets

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seq ID	L/R chain	CDR3																				alt. CDR3																				
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
CA0101	parental	E	V	Q	L	Q	S	G	P	E	L	V	F	E	K	S	G	S	G	S	G	E	V	K	S	G	S	G	S	G	S	G	S	G	S	G	S	G	S	G	S	G
human acceptor A		Q	V	Q	L	V	Q	S	S	A	S	V	E	E	S	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab1	h0101-L080	Q	V	Q	L	V	Q	S	S	A	E	V	K	E	E	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab2	h0101-L081	Q	V	Q	L	V	Q	S	S	A	E	V	K	E	E	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab3	h0101-L082	Q	V	Q	L	V	Q	S	S	A	E	V	K	E	E	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab4	h0101-L109	Q	V	Q	L	V	Q	S	S	A	E	V	K	E	E	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab5	h0101-L181	Q	V	Q	L	V	Q	S	S	A	E	V	K	E	E	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab6	h0101-L182	Q	V	Q	L	V	Q	S	S	A	E	V	K	E	E	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
CA0102	parental	E	V	Q	L	Q	S	G	P	E	L	V	K	P	E	K	S	G	S	G	S	E	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
human acceptor B		Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab7	h0102-L083	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab8	h0102-L181	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab9	h0102-L084	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab10	h0102-L082	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab11	h0102-L182	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab12	h0102-L282	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
CA0111	parental	E	V	Q	L	Q	S	G	P	E	L	V	K	P	E	K	S	G	S	G	S	E	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
human acceptor C		Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab13	h0111-L081	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab14	h0111-L181	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab15	h0111-L082	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
Ab16	h0111-L182	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	S	S	S	S	S	S	C	V	K	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	

FIG. 1A

Ab ID		L/H chains		CD832																				
Ab0301	parental	S	L	E	N	I	G	D	I	N	P	Y	N	G	G	T	T	F	N	Q	K	P	K	G
human acceptor A		G	L	X	N	N	G	D	I	N	P	Y	N	Q	G	T	T	F	N	Q	K	P	K	G
Ab1	h0301-L0H0	G	L	X	N	N	G	D	I	N	P	Y	N	Q	G	T	T	F	N	Q	K	P	K	G
Ab2	h0301-L0H1	G	L	E	N	N	G	D	I	N	P	Y	N	Q	G	T	T	F	N	Q	K	P	K	G
Ab3	h0301-L0H2	G	L	E	N	N	G	D	I	N	P	Y	N	Q	G	T	T	F	N	Q	K	P	K	G
Ab4	h0301-L0H3	G	L	E	N	N	G	D	I	N	P	Y	N	Q	G	T	T	F	N	Q	K	P	K	G
Ab5	h0301-L0H4	G	L	E	N	N	G	D	I	N	P	Y	N	Q	G	T	T	F	N	Q	K	P	K	G
Ab6	h0301-L0H5	G	L	E	N	N	G	D	I	N	P	Y	N	Q	G	T	T	F	N	Q	K	P	K	G
Ab0302	parental	G	L	E	N	I	G	E	I	N	P	Y	T	D	Y	I	V	Y	N	S	K	F	K	G
human acceptor B		G	L	E	N	N	G	E	I	N	P	Y	N	S	K	F	Y	Y	N	S	K	F	K	G
Ab7	h0302-L0H1	G	L	E	N	N	G	E	I	N	P	Y	T	D	Y	I	V	Y	N	S	K	F	K	G
Ab8	h0302-L0H2	G	L	E	N	N	G	E	I	N	P	Y	T	D	Y	I	V	Y	N	S	K	F	K	G
Ab9	h0302-L0H3	G	L	E	N	N	G	E	I	N	P	Y	T	D	Y	I	V	Y	N	S	K	F	K	G
Ab10	h0302-L0H4	G	L	E	N	N	G	E	I	N	P	Y	T	D	Y	I	V	Y	N	S	K	F	K	G
Ab11	h0302-L0H5	G	L	E	N	N	G	E	I	N	P	Y	T	D	Y	I	V	Y	N	S	K	F	K	G
Ab12	h0302-L0H2	G	L	E	N	N	G	E	I	N	P	Y	T	D	Y	I	V	Y	N	S	K	F	K	G
Ab13	parental	S	L	E	N	N	G	E	I	N	P	N	N	G	V	V	V	Y	N	Q	K	F	K	G
human acceptor C		G	L	E	N	N	G	E	I	N	P	N	N	Q	V	V	V	Y	N	Q	K	F	K	G
Ab14	h0311-L0H1	G	L	E	N	N	G	E	I	N	P	N	N	Q	V	V	V	Y	N	Q	K	F	K	G
Ab15	h0311-L0H2	G	L	E	N	N	G	E	I	N	P	N	N	Q	V	V	V	Y	N	Q	K	F	K	G
Ab16	h0311-L0H3	G	L	E	N	N	G	E	I	N	P	N	N	Q	V	V	V	Y	N	Q	K	F	K	G
Ab17	h0311-L0H4	G	L	E	N	N	G	E	I	N	P	N	N	Q	V	V	V	Y	N	Q	K	F	K	G
Ab18	h0311-L0H5	G	L	E	N	N	G	E	I	N	P	N	N	Q	V	V	V	Y	N	Q	K	F	K	G

FIG. 1B

Ab ID	L/H chain	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200	201	202	203	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336	337	338	339	340	341	342	343	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359	360	361	362	363	364	365	366	367	368	369	370	371	372	373	374	375	376	377	378	379	380	381	382	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440	441	442	443	444	445	446	447	448	449	450	451	452	453	454	455	456	457	458	459	460	461	462	463	464	465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525	526	527	528	529	530	531	532	533	534	535	536	537	538	539	540	541	542	543	544	545	546	547	548	549	550	551	552	553	554	555	556	557	558	559	560	561	562	563	564	565	566	567	568	569	570	571	572	573	574	575	576	577	578	579	580	581	582	583	584	585	586	587	588	589	590	591	592	593	594	595	596	597	598	599	600	601	602	603	604	605	606	607	608	609	610	611	612	613	614	615	616	617	618	619	620	621	622	623	624	625	626	627	628	629	630	631	632	633	634	635	636	637	638	639	640	641	642	643	644	645	646	647	648	649	650	651	652	653	654	655	656	657	658	659	660	661	662	663	664	665	666	667	668	669	670	671	672	673	674	675	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	691	692	693	694	695	696	697	698	699	700	701	702	703	704	705	706	707	708	709	710	711	712	713	714	715	716	717	718	719	720	721	722	723	724	725	726	727	728	729	730	731	732	733	734	735	736	737	738	739	740	741	742	743	744	745	746	747	748	749	750	751	752	753	754	755	756	757	758	759	760	761	762	763	764	765	766	767	768	769	770	771	772	773	774	775	776	777	778	779	780	781	782	783	784	785	786	787	788	789	790	791	792	793	794	795	796	797	798	799	800	801	802	803	804	805	806	807	808	809	810	811	812	813	814	815	816	817	818	819	820	821	822	823	824	825	826	827	828	829	830	831	832	833	834	835	836	837	838	839	840	841	842	843	844	845	846	847	848	849	850	851	852	853	854	855	856	857	858	859	860	861	862	863	864	865	866	867	868	869	870	871	872	873	874	875	876	877	878	879	880	881	882	883	884	885	886	887	888	889	890	891	892	893	894	895	896	897	898	899	900	901	902	903	904	905	906	907	908	909	910	911	912	913	914	915	916	917	918	919	920	921	922	923	924	925	926	927	928	929	930	931	932	933	934	935	936	937	938	939	940	941	942	943	944	945	946	947	948	949	950	951	952	953	954	955	956	957	958	959	960	961	962	963	964	965	966	967	968	969	970	971	972	973	974	975	976	977	978	979	980	981	982	983	984	985	986	987	988	989	990	991	992	993	994	995	996	997	998	999	1000	1001	1002	1003	1004	1005	1006	1007	1008	1009	1010	1011	1012	1013	1014	1015	1016	1017	1018	1019	1020	1021	1022	1023	1024	1025	1026	1027	1028	1029	1030	1031	1032	1033	1034	1035	1036	1037	1038	1039	1040	1041	1042	1043	1044	1045	1046	1047	1048	1049	1050	1051	1052	1053	1054	1055	1056	1057	1058	1059	1060	1061	1062	1063	1064	1065	1066	1067	1068	1069	1070	1071	1072	1073	1074	1075	1076	1077	1078	1079	1080	1081	1082	1083	1084	1085	1086	1087	1088	1089	1090	1091	1092	1093	1094	1095	1096	1097	1098	1099	1100	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112	1113	1114	1115	1116	1117	1118	1119	1120	1121	1122	1123	1124	1125	1126	1127	1128	1129	1130	1131	1132	1133	1134	1135	1136	1137	1138	1139	1140	1141	1142	1143	1144	1145	1146	1147	1148	1149	1150	1151	1152	1153	1154	1155	1156	1157	1158	1159	1160	1161	1162	1163	1164	1165	1166	1167	1168	1169	1170	1171	1172	1173	1174	1175	1176	1177	1178	1179	1180	1181	1182	1183	1184	1185	1186	1187	1188	1189	1190	1191	1192	1193	1194	1195	1196	1197	1198	1199	1200	1201	1202	1203	1204	1205	1206	1207	1208	1209	1210	1211	1212	1213	1214	1215	1216	1217	1218	1219	1220	1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Ab ID	L/H chains	CH3L1																						
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20			
cAb0301	parental	N	I	V	L	T	Q	S	P	A	S	L	A	V	E	L	G	K	A	T	I	S	C	
	human acceptor D	S	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C	
	Ab1	h0301-L0H0	S	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
	Ab2	h0301-L0H1	S	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
	Ab3	h0301-L0H2	S	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
	Ab4	h0301-L1H0	N	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
	Ab5	h0301-L1H1	N	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
cAb0302	parental	N	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C	
	human acceptor E	E	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C	
	Ab7	h0302-L0H1	E	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
	Ab8	h0302-L1H1	E	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
	Ab9	h0302-L2H1	E	I	V	V	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
	Ab10	h0302-L0H2	E	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
	Ab11	h0302-L1H2	E	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
cAb 0311	parental	D	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C	
	human acceptor F	F	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C	
	Ab13	h0311-L0H1	E	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
	Ab14	h0311-L1H1	D	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
	Ab15	h0311-L0H2	E	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C
	Ab16	h0311-L1H2	D	I	V	L	T	Q	S	P	A	T	L	S	L	S	F	G	K	A	T	L	S	C

FIG. 2A

Ab ID	L/H chains	CDRL2																			
		W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
CDR0301	parental	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab1	h0301-L0H0	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab2	h0301-L0H1	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab3	h0301-L0H2	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab4	h0301-L1H0	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab5	h0301-L1H1	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab6	h0301-L1H2	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
CDR0302	parental	W	P	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
human acceptor E		W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab7	h0302-L0H1	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab8	h0302-L1H1	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab9	h0302-L2H1	W	P	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab10	h0302-L0H2	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab11	h0302-L1H2	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab12	h0302-L2H2	W	P	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
CDR0311	parental	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
human acceptor F		W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab13	h0311-L0H1	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab14	h0311-L1H1	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab15	h0311-L0H2	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q
Ab16	h0311-L1H2	W	Y	Q	Q	K	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q	P	Q	Q

FIG. 2B

Ab ID	L/H chains	CDRL3																		SEQ ID NO
		72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	
CA0301	parental	P	T	L	N	I	H	P	V	E	S	S	D	A	A	T	Y	Y	C	10
human acceptor D		F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		81-84
Ab1	h0301-L0H0	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		46
Ab2	h0301-L0H1	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		45
Ab3	h0301-L0H2	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		45
Ab4	h0301-L1H0	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		47
Ab5	h0301-L1H1	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		47
Ab6	h0301-L1H2	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		47
CA0302	parental	F	T	L	T	I	D	P	V	E	S	S	D	A	A	T	Y	Y	C	12
human acceptor E		F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		85-89
Ab7	h0302-L0H1	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		48
Ab8	h0302-L1H1	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		49
Ab9	h0302-L2H1	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		50
Ab10	h0302-L0H2	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		48
Ab11	h0302-L1H2	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		49
Ab12	h0302-L2H2	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		50
CA0311	parental	P	T	L	T	I	H	P	V	E	S	S	D	A	A	T	Y	Y	C	14
human acceptor F		F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		89-92
Ab13	h0311-L0H1	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		51
Ab14	h0311-L1H1	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		52
Ab15	h0311-L0H2	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		51
Ab16	h0311-L1H2	F	T	L	T	I	S	S	L	E	E	D	F	A	V	V	Y	C		52

FIG. 2C

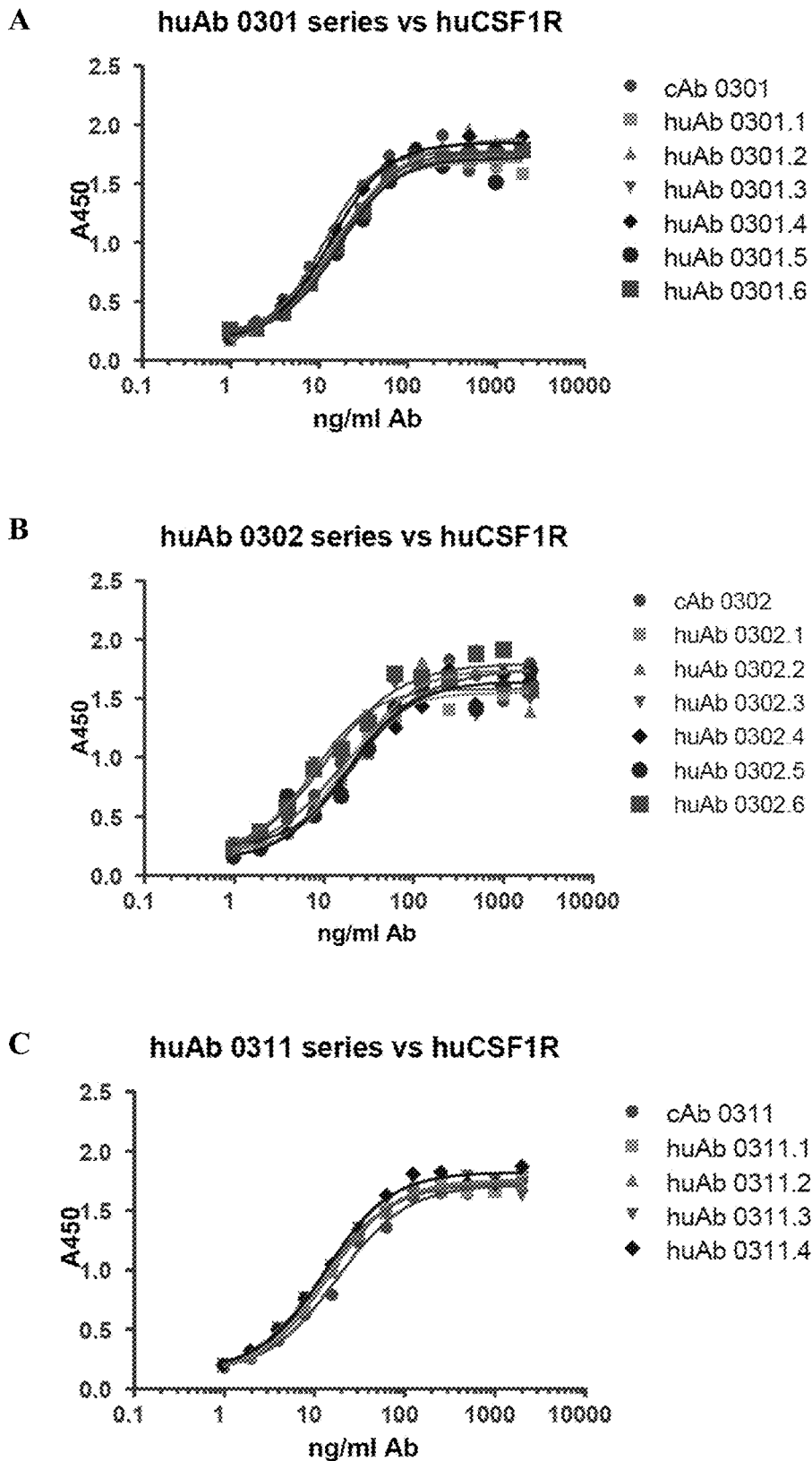


FIG. 3

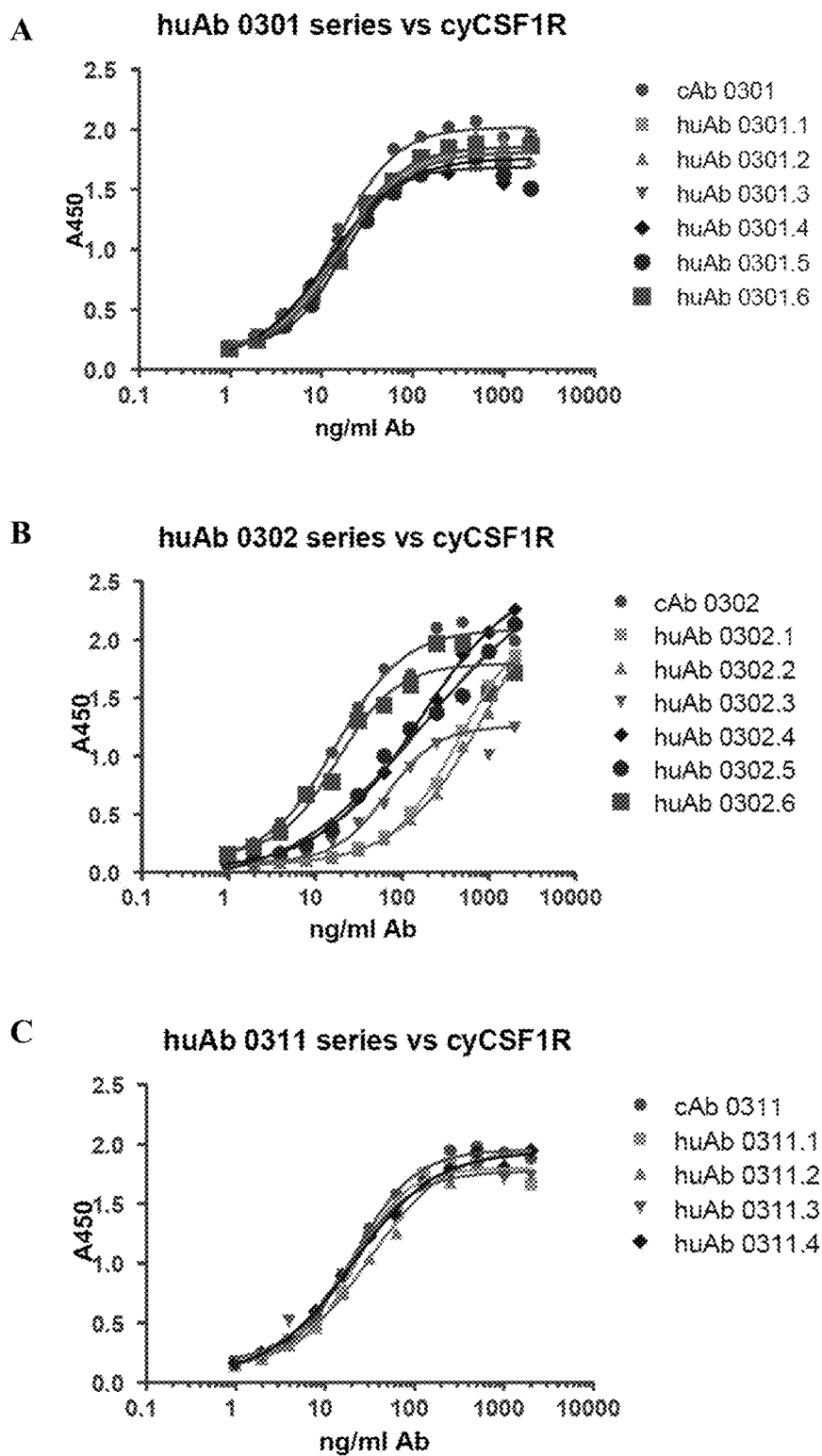


FIG. 4

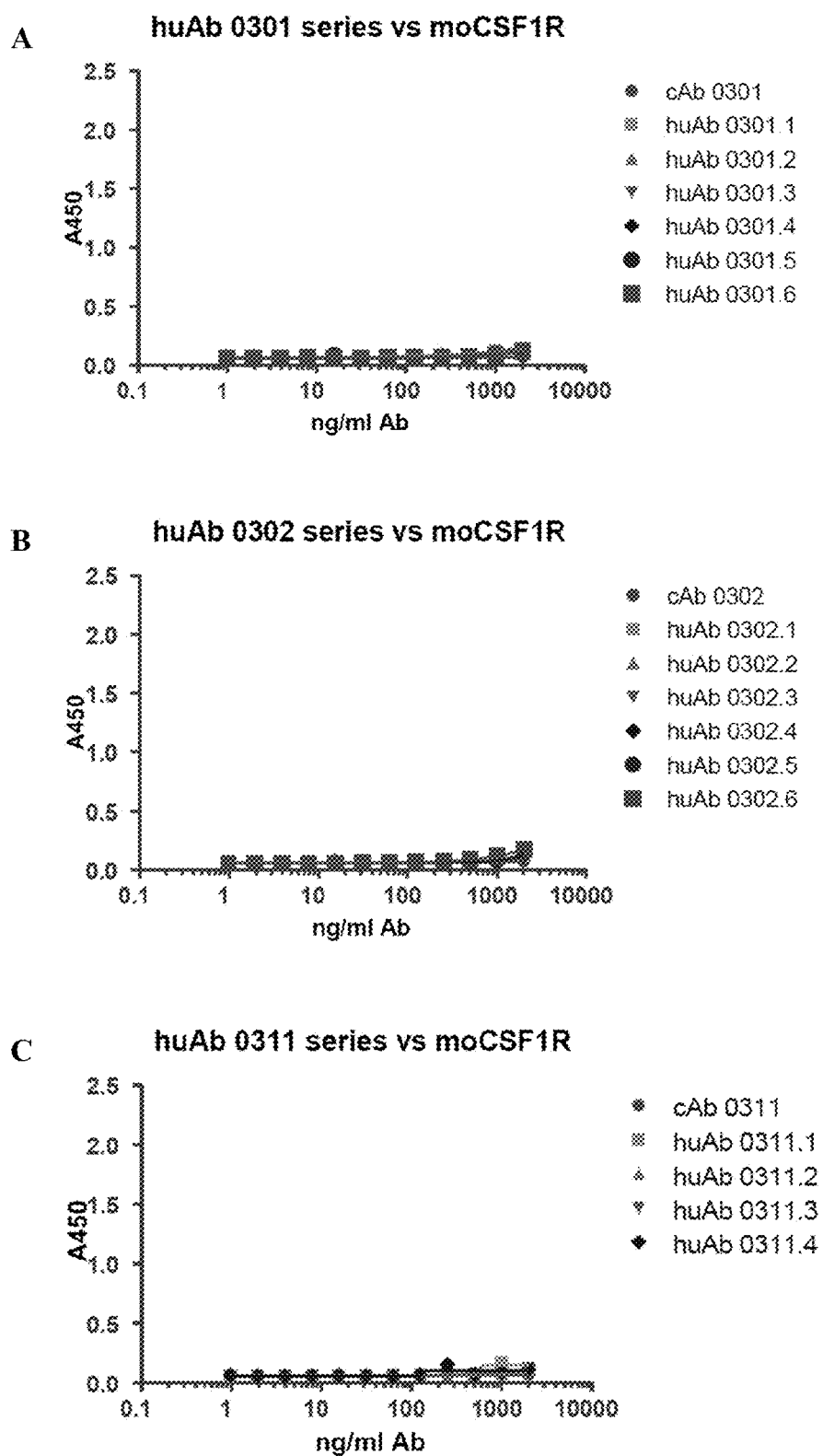


FIG. 5

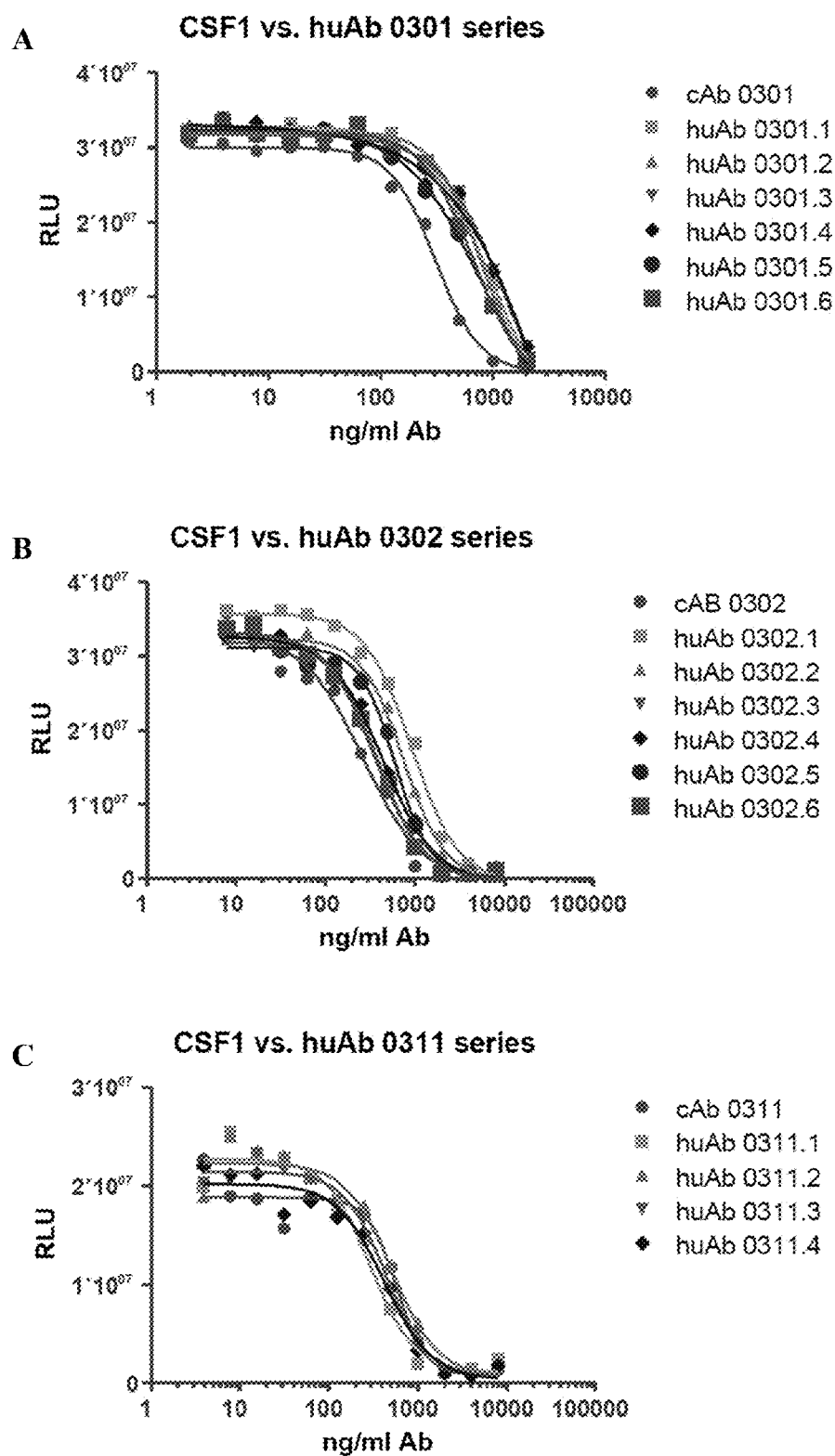


FIG. 6

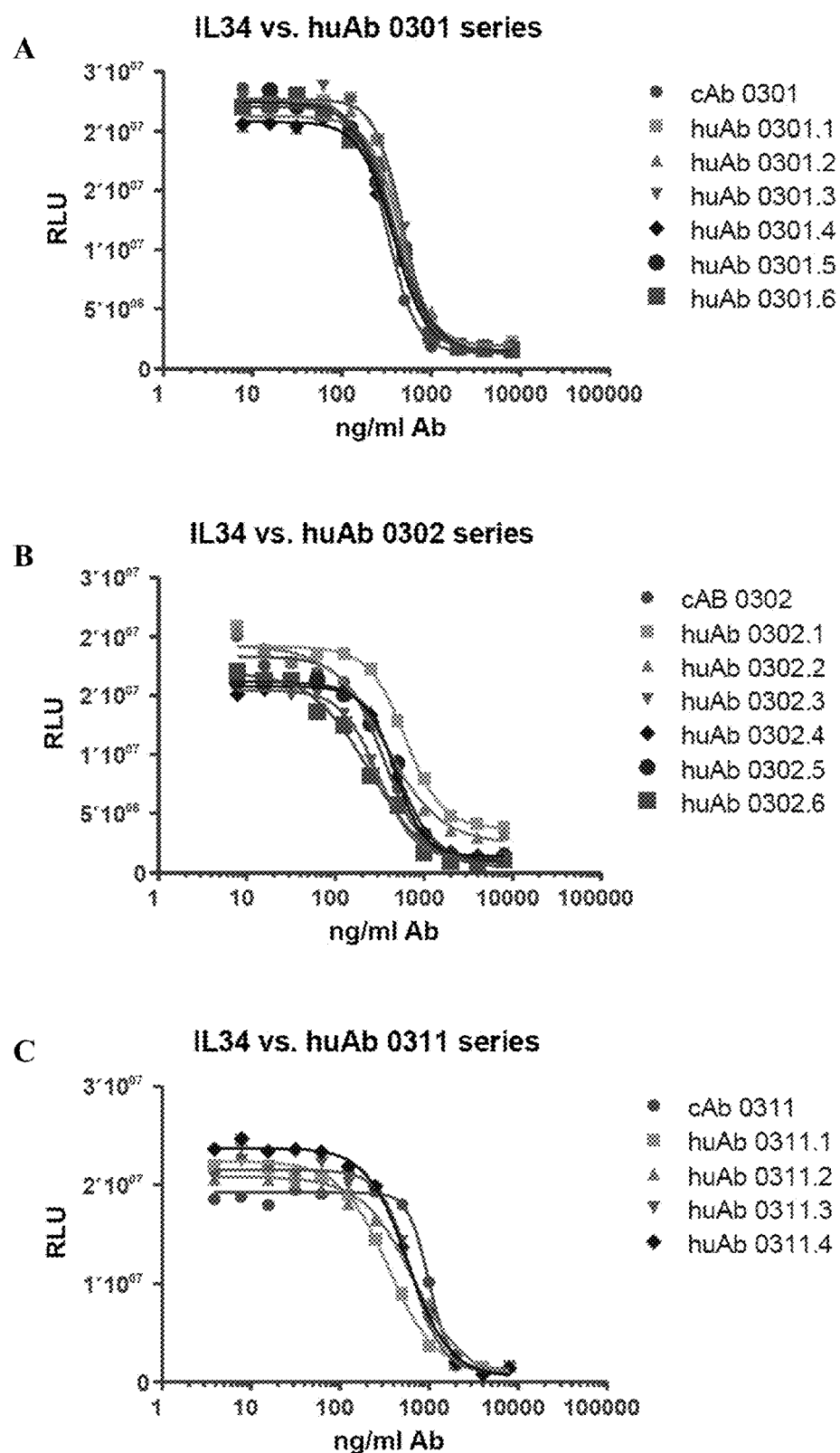
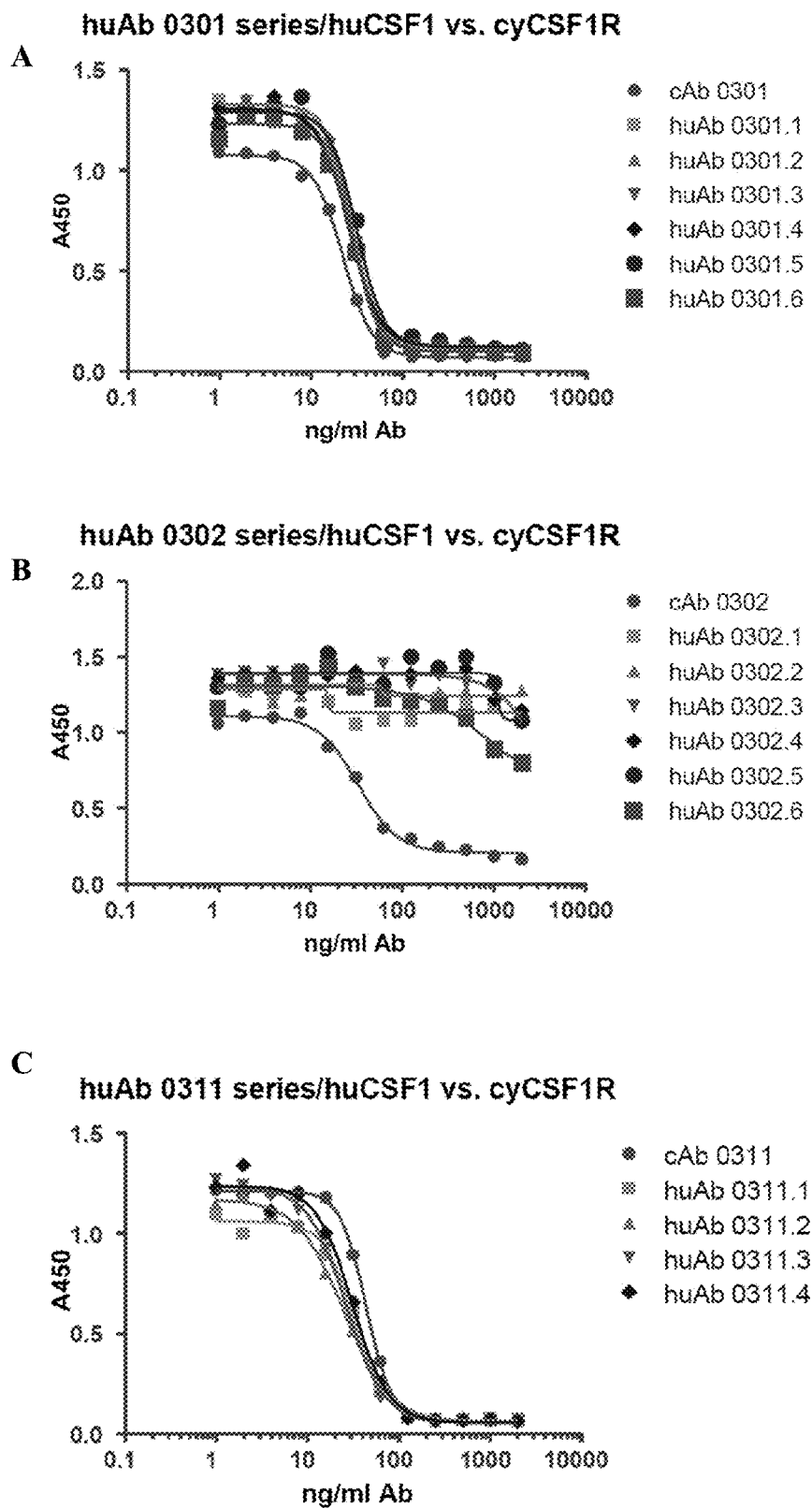


FIG. 7



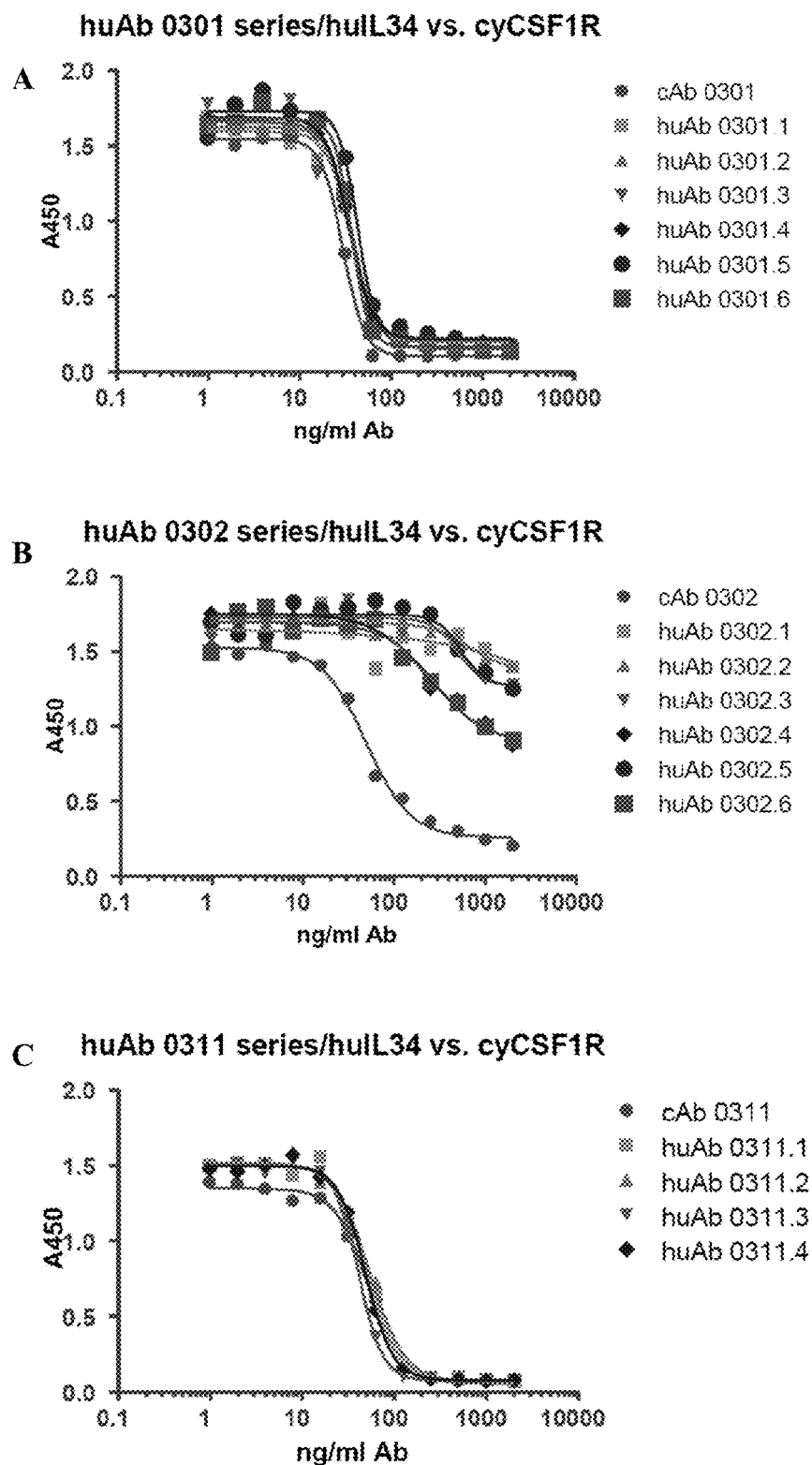


FIG. 9

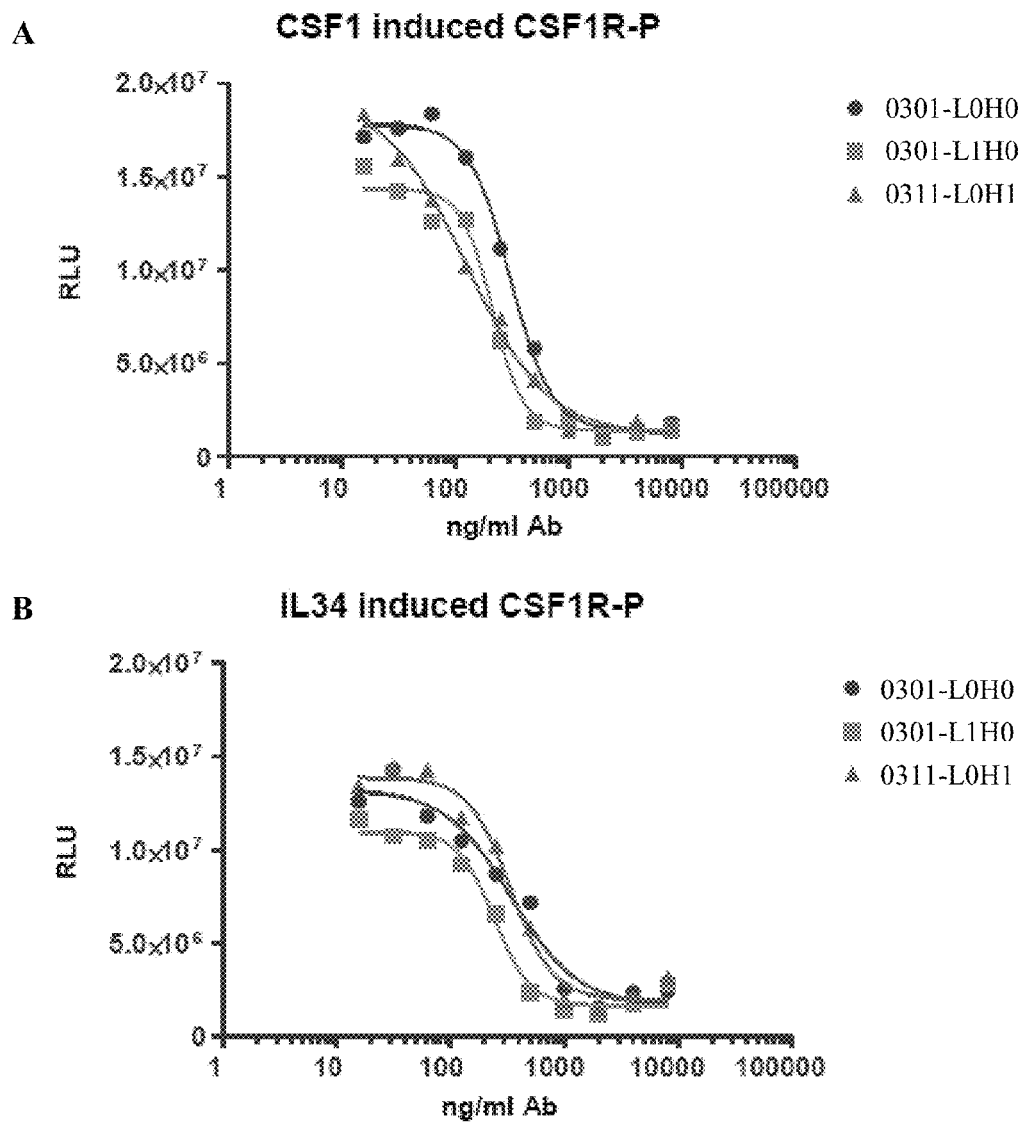


FIG. 10

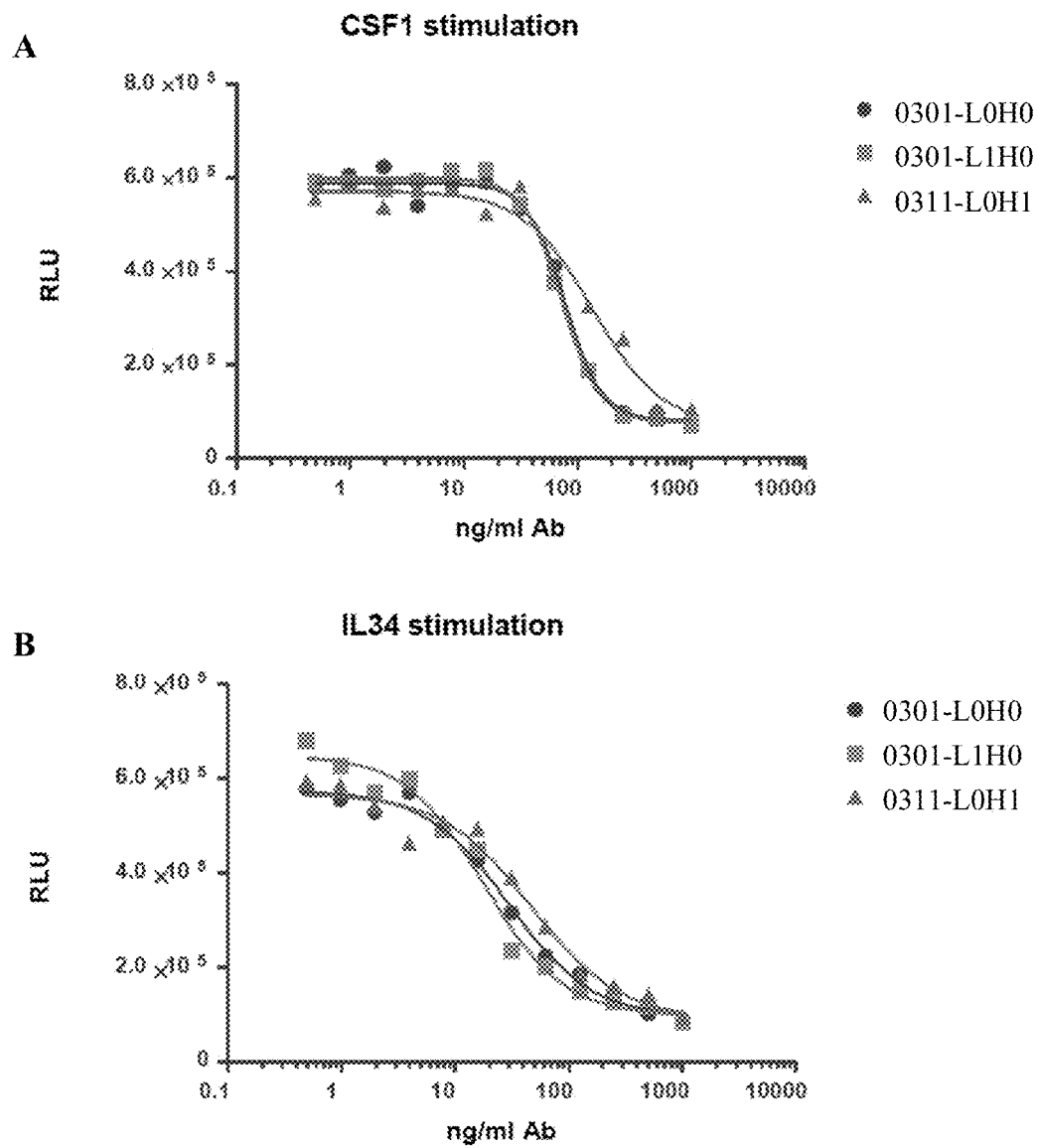


FIG. 11

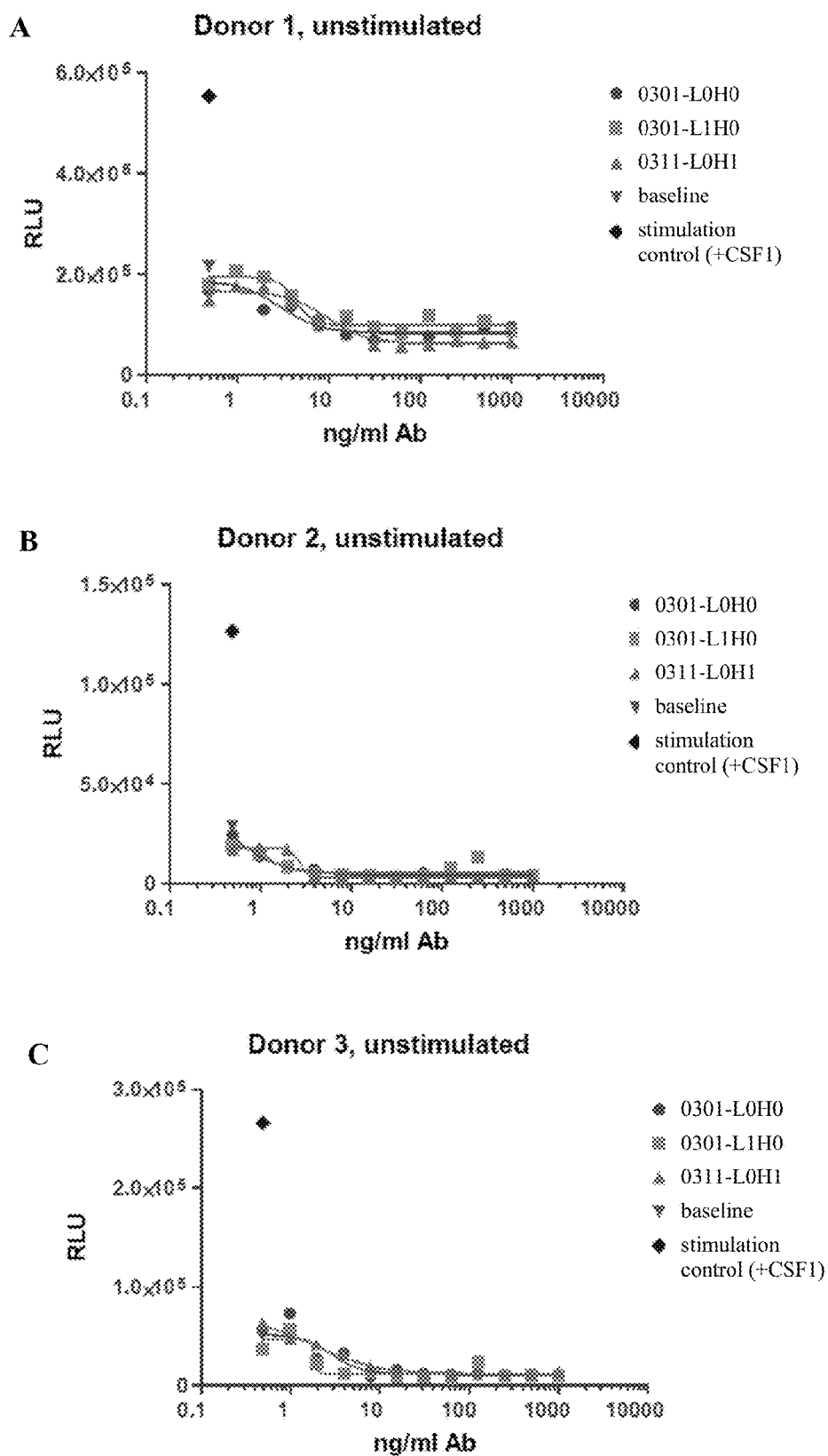


FIG. 12

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NUCLEIC ACIDS ENCODING ANTIBODIES THAT BIND COLONY STIMULATING FACTOR 1 RECEPTOR (CSF1R)

This application is a divisional of U.S. patent application Ser. No. 13/464,503, filed May 4, 2012, now U.S. Pat. No. 8,747,845, which is a divisional of U.S. patent application Ser. No. 13/100,990, filed May 4, 2011, now U.S. Pat. No. 8,206,715, which claims the benefit of U.S. Provisional Application No. 61/331,177, filed May 4, 2010, each of which is incorporated by reference herein in its entirety for any purpose.

TECHNICAL FIELD

Antibodies that bind CSF1R are provided. Antibody heavy chains and light chains that are capable of forming antibodies that bind CSF1R are also provided. In addition, antibodies, heavy chains, and light chains comprising one or more particular complementarity determining regions (CDRs) are provided. Polynucleotides encoding antibodies to CSF1R are provided. Polynucleotides encoding antibody heavy chains or light chains are also provided. Methods of treatment using antibodies to CSF1R are provided. Such methods include, but are not limited to, methods of treating rheumatoid arthritis, bone loss, and multiple sclerosis.

BACKGROUND

Colony stimulating factor 1 receptor (referred to herein as CSF1R; also referred to in the art as FMS, FIM2, C-FMS, and CD115) is a single-pass transmembrane receptor with an N-terminal extracellular domain (ECD) and a C-terminal intracellular domain with tyrosine kinase activity. Ligand binding of CSF1 or the interleukin 34 ligand (referred to herein as IL34; Lin et al., *Science* 320: 807-11 (2008)) to CSF1R leads to receptor dimerization, upregulation of CSF1R protein tyrosine kinase activity, phosphorylation of CSF1R tyrosine residues, and downstream signaling events. Both CSF1 and IL34 stimulate monocyte survival, proliferation, and differentiation into macrophages.

Many tumor cells have been found to secrete CSF1, which activates monocyte/macrophage cells through CSF1R. The level of CSF1 in tumors has been shown to correlate with the level of tumor-associated macrophages (TAMs) in the tumor. Higher levels of TAMs have been found to correlate with poorer patient prognoses. In addition, CSF1 has been found to promote tumor growth and progression to metastasis in, for example, human breast cancer xenografts in mice. See, e.g., Paulus et al., *Cancer Res.* 66: 4349-56 (2006). Further, CSF1R appears to play a role in osteolytic bone destruction in bone metastasis, as a small molecule inhibitor of receptor tyrosine kinase activity suppresses that destruction. See, e.g., Ohno et al., *Mol. Cancer Ther.* 5: 2634-43 (2006).

CSF1 and its receptor have also been found to be involved in various inflammatory and autoimmune diseases. See, e.g., Hamilton, *Nat. Rev.* 8: 533-44 (2008). For example, synovial endothelial cells from joints afflicted with rheumatoid arthritis have been found to produce CSF1, suggesting a role for CSF1 and its receptor in the disease. Blocking CSF1R activity with an antibody results in positive clinical effects in mouse models of arthritis, including a reduction in the destruction of bone and cartilage and a reduction in macrophage numbers. See, e.g., Kitaura et al., *J. Clin. Invest.* 115: 3418-3427 (2005).

Mature differentiated myeloid lineage cells such as macrophages, microglial cells, and osteoclasts contribute to

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pathology of various diseases such as rheumatoid arthritis, multiple sclerosis and diseases of bone loss. Differentiated myeloid lineage cells are derived from peripheral blood monocyte intermediates. CSF1R stimulation contributes to development of monocytes from bone marrow precursors, to monocyte proliferation and survival, and to differentiation of peripheral blood monocytes into differentiated myeloid lineage cells such as macrophages, microglial cells, and osteoclasts. CSF1R stimulation thus contributes to proliferation, survival, activation, and maturation of differentiated myeloid lineage cells, and in the pathologic setting, CSF1R stimulation contributes to the ability of differentiated myeloid lineage cells to mediate disease pathology.

Additional antagonists of CSF1R signaling would therefore be useful in the treatment of various CSF1R-related diseases, such as cancer, inflammatory conditions, and autoimmune diseases.

SUMMARY

The present inventors have invented a new set of antibodies, including humanized antibodies, directed against human CSF1R extracellular domain (CSF1R ECD). A Fab phage display library was made from spleens of mice that were immunized with a human CSF1R ECD-Fc fusion protein. 1056 phage clones expressing Fabs that bind to CSF1R ECD-Fc were isolated through panning of this library. When the 1056 Fabs were expressed as purified protein, 668 were found to bind to CSF1R ECD. Of those 668 binding Fabs, only 121 Fabs blocked binding of CSF1 and/or IL34 to CSF1R. Only 33 of those Fabs were found to block binding of both CSF1 and IL34 to CSF1R. Upon sequencing, the 33 Fabs represented 19 unique sets of sequences. Eleven Fabs with subnanomolar affinity for human CSF1R ECD were chosen to make chimeric antibodies for further study. Based on the human and cynomolgus monkey CSF1R binding affinities, blocking of CSF1 and IL34 binding to CSF1R, and inhibition of ligand-induced phosphorylation of CSF1R, three chimeric antibodies were selected for humanization, and sixteen humanized antibodies were made based on those three chimeric antibodies.

Fourteen of the sixteen humanized antibodies retained subnanomolar binding affinities for human CSF1R ECD. See, e.g., Table 5. These humanized antibodies block binding of both ligands CSF1 and IL34 to human CSF1R, and many also block binding of both CSF1 and IL34 to cynomolgus monkey CSF1R. See, e.g., Table 4.

For therapeutic drug development, it is beneficial to have antibodies that bind to both human and cynomolgus monkey antigens with similar affinity. The three chimeric antibodies chosen for humanization were selected in part because they had similar binding affinities for human and cynomolgus CSF1R ECD. Most of the humanized versions of one of the chimeric antibodies, 0302, however, lost significant binding affinity for cynomolgus monkey CSF1R ECD upon humanization, although they retained strong human CSF1R ECD binding affinity. See, e.g., Table 3. Humanized versions of 0301 and 0311 retained similarly strong binding to both human and cynomolgus monkey CSF1R ECD, with binding affinity differences for the two species of less than about 2-fold.

Based on CSF1R binding affinities, ligand inhibition, and the potential for immunogenicity, three humanized antibodies were selected for additional studies. The three humanized antibodies were derived from the two chimeric antibodies that did not significantly lose cynomolgus monkey CSF1R binding affinity upon humanization. Those three humanized anti-

bodies inhibit ligand-induced phosphorylation of human CSF1R, and also block ligand-induced proliferation and survival responses in primary human monocytes. See, e.g., Tables 6 and 7, and FIGS. 10 and 11. Thus, these antibodies are useful for treating diseases involving, for example, ligand-induced proliferation and survival responses in primary human monocytes.

Blocking CSF1R-induced responses with an anti-CSF1R antibody should inhibit proliferation, survival, activation, maturation of differentiated myeloid lineage cells and attenuate their ability to mediate disease pathology. In addition, blocking CSF1R-induced responses with an anti-CSF1R antibody should inhibit differentiation of peripheral blood monocyte intermediates into differentiated myeloid lineage cells, decreasing the number of pathology-mediating differentiated myeloid lineage cells.

Accordingly, the humanized anti-CSF1R antibodies described herein can be used to treat chronic diseases with extant symptoms by inhibiting the ability of differentiated myeloid lineage cells to mediate disease pathology. The humanized antibodies can also be used to treat chronic diseases that are relapsing and remitting in nature by inhibiting the development of new pathology-mediating myeloid lineage cells differentiated from peripheral blood monocytes during the remitting phase of the disease, thus attenuating the number of and new formation of the pathology-mediating cells.

In some embodiments, an isolated antibody comprising a heavy chain and a light chain is provided, wherein the antibody binds to CSF1R. In some embodiments, the heavy chain and/or light chain have the following structure.

In some embodiments, the heavy chain comprises a sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45. In some embodiments, the light chain comprises a sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52. In some embodiments, the heavy chain comprises a sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45, and the light chain comprises a sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52.

In some embodiments, the HC CDR1, HC CDR2, and HC CDR3 comprise a set of sequences selected from: (a) SEQ ID NOs: 15, 16, and 17; (b) SEQ ID NOs: 21, 22, and 23; and (c) SEQ ID NOs: 27, 28, and 29. In some embodiments, the LC CDR1, LC CDR2, and LC CDR3 comprise a set of sequences selected from: (a) SEQ ID NOs: 18, 19, and 20; (b) SEQ ID NOs: 24, 25, and 26; and (c) SEQ ID NOs: 30, 31, and 32.

In some embodiments, the heavy chain comprises an HC CDR1, HC CDR2, and HC CDR3, wherein the HC CDR1, HC CDR2, and HC CDR3 comprise a set of sequences selected from: (a) SEQ ID NOs: 15, 16, and 17; (b) SEQ ID NOs: 21, 22, and 23; and (c) SEQ ID NOs: 27, 28, and 29; and the light chain comprises an LC CDR1, LC CDR2, and LC CDR3, wherein the LC CDR1, LC CDR2, and LC CDR3 comprise a set of sequences selected from: (a) SEQ ID NOs: 18, 19, and 20; (b) SEQ ID NOs: 24, 25, and 26; and (c) SEQ ID NOs: 30, 31, and 32.

In some embodiments, an isolated antibody is provided, wherein the antibody comprises a heavy chain and a light chain, wherein the antibody comprises:

(a) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO:

9 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 10;

(b) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 11 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 12;

(c) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 13 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 14;

(d) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 39 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 46;

(e) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 40 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 46;

(f) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 41 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 46;

(g) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 39 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 47;

(h) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 40 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 47;

(i) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 41 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 47;

and (j) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 42 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 48;

(k) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 42 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 49;

(l) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 42 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 50;

(m) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 43 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 48;

(n) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO:

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43 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 49;

(O) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 43 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 50;

(p) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 44 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 51;

(q) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 44 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 52;

(r) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 45 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 51;

or (s) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 45 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 52.

In some embodiments, an antibody is provided, wherein the antibody comprises a heavy chain and a light chain, wherein the antibody comprises: (a) a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 15, an HC CDR2 having the sequence of SEQ ID NO: 16, and an HC CDR3 having the sequence of SEQ ID NO: 17, and a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 18, a LC CDR2 having the sequence of SEQ ID NO: 19, and a LC CDR3 having the sequence of SEQ ID NO: 20; (b) a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 21, an HC CDR2 having the sequence of SEQ ID NO: 22, and an HC CDR3 having the sequence of SEQ ID NO: 23, and a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 24, a LC CDR2 having the sequence of SEQ ID NO: 25, and a LC CDR3 having the sequence of SEQ ID NO: 26; or (c) a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 27, an HC CDR2 having the sequence of SEQ ID NO: 28, and an HC CDR3 having the sequence of SEQ ID NO: 29, and a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 30, a LC CDR2 having the sequence of SEQ ID NO: 31, and a LC CDR3 having the sequence of SEQ ID NO: 32.

In some embodiments, an antibody comprises a heavy chain and a light chain, wherein the antibody comprises: (a) a heavy chain comprising a sequence of SEQ ID NO: 53 and a light chain comprising a sequence of SEQ ID NO: 60; (b) a heavy chain comprising a sequence of SEQ ID NO: 53 and a light chain comprising a sequence of SEQ ID NO: 61; or (c) a heavy chain comprising a sequence of SEQ ID NO: 58 and a light chain comprising a sequence of SEQ ID NO: 65. In some embodiments, an antibody comprises a heavy chain and a light chain, wherein the antibody comprises: (a) a heavy chain consisting of the sequence of SEQ ID NO: 53 and a light chain consisting of the sequence of SEQ ID NO: 60; (b) a heavy chain consisting of the sequence of SEQ ID NO: 53 and a light chain consisting of the sequence of SEQ ID NO: 61; or

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(c) a heavy chain consisting of the sequence of SEQ ID NO: 58 and a light chain consisting of the sequence of SEQ ID NO: 65.

In some embodiments, an antibody is a humanized antibody. In some embodiments, an antibody is selected from a Fab, an Fv, an scFv, a Fab', and a (Fab')₂. In some embodiments, an antibody is a chimeric antibody. In some embodiments, an antibody is selected from an IgA, an IgG, and an IgD. In some embodiments, an antibody is an IgG. In some embodiments, an antibody is an IgG4. In some embodiments, an antibody is an IgG4 comprising an S241P mutation in at least one IgG4 heavy chain constant region.

In some embodiments, an antibody binds to human CSF1R and/or binds to cynomolgus CSF1R. In some embodiments, an antibody blocks ligand binding to CSF1R. In some embodiments, an antibody blocks binding of CSF1 and/or IL34 to CSF1R. In some embodiments, an antibody inhibits ligand-induced CSF1R phosphorylation. In some embodiments, an antibody inhibits CSF1- and/or IL34-induced CSF1R phosphorylation. In some embodiments, an antibody binds to human CSF1R with an affinity (K_D) of less than 1 nM. In some embodiments, antibody inhibits monocyte proliferation and/or survival responses in the presence of CSF1 or IL34.

In some embodiments, a pharmaceutical composition comprising an antibody that binds CSF1R is provided.

In some embodiments, an isolated nucleic acid is provided, wherein the isolated nucleic acid comprises a polynucleotide sequence that encodes a heavy chain described above. In some embodiments, an isolated nucleic acid encodes a light chain described above. In some embodiments, an isolated nucleic acid encodes a heavy chain described above and a light chain described above. In some embodiments, a composition is provided, wherein the composition comprises a first nucleic acid that comprises a polynucleotide sequence that encodes a heavy chain described above, and a second nucleic acid that comprises a polynucleotide sequence that encodes a light chain described above. In some embodiments, a host cell comprising a nucleic acid or a composition described above is provided. In some embodiments, a host cell is a eukaryotic host cell. In some embodiments, a host cell is a mammalian host cell. In some embodiments, a host cell is selected from a CHO cell, a 293 cell, an NSO cell, and a PER.C6 cell. In some embodiments, a host cell is a 293-6E cell or a DG44 cell.

In some embodiments, methods of treating disease comprising administering to a patient a pharmaceutical composition comprising an antibody that binds CSF1R is provided. In some embodiments, a method of treating multiple sclerosis comprising administering to a patient a pharmaceutical composition comprising an antibody that binds CSF1R is provided. In some embodiments, a method of treating rheumatoid arthritis comprising administering to a patient a pharmaceutical composition comprising an antibody that binds CSF1R is provided. In some embodiments, a method of treating osteolytic bone loss comprising administering to a patient a pharmaceutical composition comprising an antibody that binds CSF1R is provided. In some embodiments, the osteolytic bone loss is selected from osteoporosis, metastasis-induced osteolytic bone loss, and rheumatoid arthritis-induced bone loss. In some embodiments, a method of treating cancer comprising administering to a patient a pharmaceutical composition comprising an antibody that binds CSF1R is provided. In some embodiments, the cancer is selected from breast cancer, prostate cancer, endometrial cancer, bladder cancer, kidney cancer, esophageal cancer, squamous cell carcinoma, uveal melanoma, follicular lymphoma,

renal cell carcinoma, cervical cancer, ovarian cancer, lung cancer, colorectal cancer, brain cancer, pancreatic cancer, head and neck cancer, liver cancer, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, melanoma, astrocytoma, stomach cancer, and pulmonary adenocarcinoma.

In some embodiments, a method of treating an inflammatory condition comprising administering to a patient a pharmaceutical composition comprising an antibody that binds CSF1R is provided.

In some embodiments, antibodies that bind CSF1R and compositions comprising antibodies that bind CSF1R are provided for use in methods of treatment of human or animals. In some embodiments, antibodies that bind CSF1R and compositions comprising antibodies that bind CSF1R are provided for use in a method of treating rheumatoid arthritis in a human or animal. In some embodiments, antibodies that bind CSF1R and compositions comprising antibodies that bind CSF1R are provided for use in a method of treating multiple sclerosis in a human or animal. In some embodiments, antibodies that bind CSF1R and compositions comprising antibodies that bind CSF1R are provided for use in a method of treating cancer in a human or animal. In some embodiments, antibodies that bind CSF1R and compositions comprising antibodies that bind CSF1R are provided for use in a method of treating an inflammatory condition in a human or animal.

BRIEF DESCRIPTION OF THE FIGURES

FIGS. 1A-C show an alignment of the humanized heavy chain variable regions for each of humanized antibodies Ab1 to Ab16, as discussed in Example 4. Boxed residues are amino acids in the human acceptor sequence that were changed back to the corresponding mouse residue.

FIGS. 2A-C show an alignment of the humanized light chain variable regions for each of humanized antibodies Ab1 to Ab16, as discussed in Example 4. Boxed amino acids are residues in the human acceptor sequence that were changed back to the corresponding mouse residue.

FIGS. 3A-C show binding curves for certain humanized antibodies binding to human CSF1R ECD, as described in Example 5. FIG. 3A shows binding curves for parental chimeric antibodies (cAb) 0301 and humanized antibodies (huAb) 0301.1, 0301.2, 0302.3, 0301.4, 0301.5, and 0301.6 (h0301-L0H0, h0301-L0H1, h0301-L0H2, h0301-L1H0, h0301-L1H1, and h0301-L1H2, respectively). FIG. 3B shows binding curves for parental cAb 0302 and humanized antibodies (huAb) 0302.1, 0302.2, 0302.3, 0302.4, 0302.5, and 0302.6 (h0302-L0H1, h0302-L1H1, h0302-L2H1, h0302-L0H2, h0302-L1H2, and h0302-L2H2, respectively). FIG. 3C shows binding curves for parental cAb 0311 and humanized antibodies (huAb) 0311.1, 0311.2, 0311.3, and 0311.4 (h0311-L0H1, h0311-L1H1, h0311-L0H2, and h0311-L1H2, respectively).

FIGS. 4A-C show binding curves for certain humanized antibodies binding to cynomolgus CSF1R ECD, as described in Example 5. FIG. 4A shows binding curves for parental cAb 0301 and humanized antibodies (huAb) 0301.1, 0301.2, 0302.3, 0301.4, 0301.5, and 0301.6 (h0301-L0H0, h0301-L0H1, h0301-L0H2, h0301-L1H0, h0301-L1H1, and h0301-L1H2, respectively). FIG. 4B shows binding curves for parental cAb 0302 and humanized antibodies (huAb) 0302.1, 0302.2, 0302.3, 0302.4, 0302.5, and 0302.6 (h0302-L0H1, h0302-L1H1, h0302-L2H1, h0302-L0H2, h0302-L1H2, and h0302-L2H2, respectively). FIG. 4C shows binding curves for parental cAb 0311 and humanized antibodies (huAb)

0311.1, 0311.2, 0311.3, and 0311.4 (h0311-L0H1, h0311-L1H1, h0311-L0H2, and h0311-L1H2, respectively).

FIGS. 5A-C show binding curves for certain humanized antibodies binding to mouse CSF1R ECD, as described in Example 5. FIG. 5A shows binding curves for parental cAb 0301 and humanized antibodies (huAb) 0301.1, 0301.2, 0302.3, 0301.4, 0301.5, and 0301.6 (h0301-L0H0, h0301-L0H1, h0301-L0H2, h0301-L1H0, h0301-L1H1, and h0301-L1H2, respectively). FIG. 5B shows binding curves for parental cAb 0302 and humanized antibodies (huAb) 0302.1, 0302.2, 0302.3, 0302.4, 0302.5, and 0302.6 (h0302-L0H1, h0302-L1H1, h0302-L2H1, h0302-L0H2, h0302-L1H2, and h0302-L2H2, respectively). FIG. 5C shows binding curves for parental cAb 0311 and humanized antibodies (huAb) 0311.1, 0311.2, 0311.3, and 0311.4 (h0311-L0H1, h0311-L1H1, h0311-L0H2, and h0311-L1H2, respectively).

FIGS. 6A-C show inhibition of CSF1 induced CSF1R phosphorylation by certain humanized antibodies, as described in Example 6. FIG. 6A shows blocking curves for parental cAb 0301 and humanized antibodies (huAb) 0301.1, 0301.2, 0302.3, 0301.4, 0301.5, and 0301.6 (h0301-L0H0, h0301-L0H1, h0301-L0H2, h0301-L1H0, h0301-L1H1, and h0301-L1H2, respectively). FIG. 6B shows blocking curves for parental cAb 0302 and humanized antibodies (huAb) 0302.1, 0302.2, 0302.3, 0302.4, 0302.5, and 0302.6 (h0302-L0H1, h0302-L1H1, h0302-L2H1, h0302-L0H2, h0302-L1H2, and h0302-L2H2, respectively). FIG. 6C shows blocking curves for parental cAb 0311 and humanized antibodies (huAb) 0311.1, 0311.2, 0311.3, and 0311.4 (h0311-L0H1, h0311-L1H1, h0311-L0H2, and h0311-L1H2, respectively).

FIGS. 7A-C show inhibition of IL34 induced CSF1R phosphorylation by certain humanized antibodies, as described in Example 6. FIG. 7A shows blocking curves for parental cAb 0301 and humanized antibodies (huAb) 0301.1, 0301.2, 0302.3, 0301.4, 0301.5, and 0301.6 (h0301-L0H0, h0301-L0H1, h0301-L0H2, h0301-L1H0, h0301-L1H1, and h0301-L1H2, respectively). FIG. 7B shows blocking curves for parental cAb 0302 and humanized antibodies (huAb) 0302.1, 0302.2, 0302.3, 0302.4, 0302.5, and 0302.6 (h0302-L0H1, h0302-L1H1, h0302-L2H1, h0302-L0H2, h0302-L1H2, and h0302-L2H2, respectively). FIG. 7C shows blocking curves for parental cAb 0311 and humanized antibodies (huAb) 0311.1, 0311.2, 0311.3, and 0311.4 (h0311-L0H1, h0311-L1H1, h0311-L0H2, and h0311-L1H2, respectively).

FIGS. 8A-C show blocking of human CSF1 binding to cynomolgus CSF1R ECD by certain humanized antibodies, as described in Example 7. FIG. 8A shows blocking curves for parental cAb 0301 and humanized antibodies (huAb) 0301.1, 0301.2, 0302.3, 0301.4, 0301.5, and 0301.6 (h0301-L0H0, h0301-L0H1, h0301-L0H2, h0301-L1H0, h0301-L1H1, and h0301-L1H2, respectively). FIG. 8B shows blocking curves for parental cAb 0302 and humanized antibodies (huAb) 0302.1, 0302.2, 0302.3, 0302.4, 0302.5, and 0302.6 (h0302-L0H1, h0302-L1H1, h0302-L2H1, h0302-L0H2, h0302-L1H2, and h0302-L2H2, respectively). FIG. 8C shows blocking curves for parental cAb 0311 and humanized antibodies (huAb) 0311.1, 0311.2, 0311.3, and 0311.4 (h0311-L0H1, h0311-L1H1, h0311-L0H2, and h0311-L1H2, respectively).

FIGS. 9A-C show blocking of human IL34 binding to cynomolgus CSF1R ECD by certain humanized antibodies, as described in Example 7. FIG. 9A shows blocking curves for parental cAb 0301 and humanized antibodies (huAb) 0301.1, 0301.2, 0302.3, 0301.4, 0301.5, and 0301.6 (h0301-L0H0, h0301-L0H1, h0301-L0H2, h0301-L1H0, h0301-L1H1, and h0301-L1H2, respectively). FIG. 9B shows blocking curves for parental cAb 0302 and humanized antibodies

(huAb) 0302.1, 0302.2, 0302.3, 0302.4, 0302.5, and 0302.6 (h0302-L0H1, h0302-L1H1, h0302-L2H1, h0302-L0H2, h0302-L1H2, and h0302-L2H2, respectively). FIG. 9C shows blocking curves for parental cAb 0311 and humanized antibodies (huAb) 0311.1, 0311.2, 0311.3, and 0311.4 (h0311-L0H1, h0311-L1H1, h0311-L0H2, and h0311-L1H2, respectively).

FIGS. 10A and B show blocking of CSF1-(10A) and IL34-(10B) induced CSF1R phosphorylation in CHO cells expressing human CSF1R by humanized antibodies 0301-L0H0, 0301-L1H0, and 0311-L0H1, as described in Example 9.

FIGS. 11A and B show blocking of CSF1-(11A) and IL34-(11B) induced monocyte proliferation/survival responses by humanized antibodies 0301-L0H0, 0301-L1H0, and 0311-L0H1, as described in Example 10.

FIGS. 12A-C show that humanized antibodies 0301-L0H0, 0301-L1H0, and 0311-L0H1 do not stimulate primary monocyte proliferation or survival, using monocytes from three different donors, as described in Example 11.

DETAILED DESCRIPTION

Methods of treating diseases comprising administering novel antibodies to CSF1R are provided. All of the antibodies have binding affinities for human CSF1R ECD of less than 2 nM, and all but two of the humanized antibodies have sub-nanomolar binding affinities for human CSF1R ECD. Further, the new antibodies block binding of both CSF1 and IL34 to human CSF1R, and inhibit ligand-induced phosphorylation of human CSF1R. Many of the new antibodies also block binding of CSF1 and IL34 to cynomolgus CSF1R, which facilitates in vivo experiments to support the development of anti-CSF1R antibody therapeutics. The new antibodies are therefore well suited for therapeutic use in human diseases, including, but not limited to, cancer, autoimmune diseases, and inflammatory conditions.

The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described.

DEFINITIONS

Unless otherwise defined, scientific and technical terms used in connection with the present invention shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular.

Exemplary techniques used in connection with recombinant DNA, oligonucleotide synthesis, tissue culture and transformation (e.g., electroporation, lipofection), enzymatic reactions, and purification techniques are known in the art. Many such techniques and procedures are described, e.g., in Sambrook et al. *Molecular Cloning: A Laboratory Manual* (2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1989)), among other places. In addition, exemplary techniques for chemical syntheses, chemical analyses, pharmaceutical preparation, formulation, and delivery, and treatment of patients are also known in the art.

In this application, the use of “or” means “and/or” unless stated otherwise. In the context of a multiple dependent claim, the use of “or” refers back to more than one preceding independent or dependent claim in the alternative only. Also, terms such as “element” or “component” encompass both

elements and components comprising one unit and elements and components that comprise more than one subunit unless specifically stated otherwise.

As utilized in accordance with the present disclosure, the following terms, unless otherwise indicated, shall be understood to have the following meanings:

The terms “nucleic acid molecule” and “polynucleotide” may be used interchangeably, and refer to a polymer of nucleotides. Such polymers of nucleotides may contain natural and/or non-natural nucleotides, and include, but are not limited to, DNA, RNA, and PNA. “Nucleic acid sequence” refers to the linear sequence of nucleotides that comprise the nucleic acid molecule or polynucleotide.

The terms “polypeptide” and “protein” are used interchangeably to refer to a polymer of amino acid residues, and are not limited to a minimum length. Such polymers of amino acid residues may contain natural or non-natural amino acid residues, and include, but are not limited to, peptides, oligopeptides, dimers, trimers, and multimers of amino acid residues. Both full-length proteins and fragments thereof are encompassed by the definition. The terms also include post-expression modifications of the polypeptide, for example, glycosylation, sialylation, acetylation, phosphorylation, and the like. Furthermore, for purposes of the present invention, a “polypeptide” refers to a protein which includes modifications, such as deletions, additions, and substitutions (generally conservative in nature), to the native sequence, as long as the protein maintains the desired activity. These modifications may be deliberate, as through site-directed mutagenesis, or may be accidental, such as through mutations of hosts which produce the proteins or errors due to PCR amplification.

The term “CSF1R” refers herein to the full-length CSF1R, which includes the N-terminal ECD, the transmembrane domain, and the intracellular tyrosine kinase domain, with or without an N-terminal leader sequence. In some embodiments, the CSF1R is a human CSF1R having the amino acid sequence of SEQ ID NO: 1 or SEQ ID NO: 2.

The term “CSF1R extracellular domain” (“CSF1R ECD”) as used herein refers to a CSF1R polypeptide that lacks the intracellular and transmembrane domains. CSF1R ECDs include the full-length CSF1R ECD and CSF1R ECD fragments that are capable of binding CSF1R and/or IL34. The human full-length CSF1R ECD is defined herein as comprising either amino acids 1 to 512 (i.e., including the leader sequence) or amino acids 20 to 512 (i.e., lacking the leader sequence) of SEQ ID NO: 2. In some embodiments, a human CSF1R ECD fragment comprises amino acids 20 to 506 of SEQ ID NO: 2 (see SEQ ID NO: 5). In some embodiments, a human CSF1R fragment ends at amino acid 507, 508, 509, 510, or 511. In some embodiments, a cynoCSF1R ECD comprises the sequence of SEQ ID NO: 7 (with leader sequence) or amino acids 20 to 506 of SEQ ID NO: 7 (without leader sequence).

The term “antibody” as used herein refers to a molecule comprising at least complementarity-determining region (CDR) 1, CDR2, and CDR3 of a heavy chain and at least CDR1, CDR2, and CDR3 of a light chain, wherein the molecule is capable of binding to antigen. The term antibody includes, but is not limited to, fragments that are capable of binding antigen, such as Fv, single-chain Fv (scFv), Fab, Fab', and (Fab')₂. The term antibody also includes, but is not limited to, chimeric antibodies, humanized antibodies, and antibodies of various species such as mouse, human, cynomolgus monkey, etc.

In some embodiments, an antibody comprises a heavy chain variable region and a light chain variable region. In

some embodiments, an antibody comprises at least one heavy chain comprising a heavy chain variable region and at least a portion of a heavy chain constant region, and at least one light chain comprising a light chain variable region and at least a portion of a light chain constant region. In some embodiments, an antibody comprises two heavy chains, wherein each heavy chain comprises a heavy chain variable region and at least a portion of a heavy chain constant region, and two light chains, wherein each light chain comprises a light chain variable region and at least a portion of a light chain constant region. As used herein, a single-chain Fv (scFv), or any other antibody that comprises, for example, a single polypeptide chain comprising all six CDRs (three heavy chain CDRs and three light chain CDRs) is considered to have a heavy chain and a light chain. In some such embodiments, the heavy chain is the region of the antibody that comprises the three heavy chain CDRs and the light chain in the region of the antibody that comprises the three light chain CDRs.

The term "heavy chain variable region" as used herein refers to a region comprising heavy chain CDR1, framework (FR) 2, CDR2, FR3, and CDR3. In some embodiments, a heavy chain variable region also comprises at least a portion of an FR1 and/or at least a portion of an FR4. In some embodiments, a heavy chain CDR1 corresponds to Kabat residues 26 to 35; a heavy chain CDR2 corresponds to Kabat residues 50 to 65; and a heavy chain CDR3 corresponds to Kabat residues 95 to 102. See, e.g., Kabat Sequences of Proteins of Immunological Interest (1987 and 1991, NIH, Bethesda, Md.); and FIG. 1. In some embodiments, a heavy chain CDR1 corresponds to Kabat residues 31 to 35; a heavy chain CDR2 corresponds to Kabat residues 50 to 65; and a heavy chain CDR3 corresponds to Kabat residues 95 to 102. See id.

The term "heavy chain constant region" as used herein refers to a region comprising at least three heavy chain constant domains, C_{H1} , C_{H2} , and C_{H3} . Nonlimiting exemplary heavy chain constant regions include γ , δ , and α . Nonlimiting exemplary heavy chain constant regions also include ϵ and μ . Each heavy constant region corresponds to an antibody isotype. For example, an antibody comprising a γ constant region is an IgG antibody, an antibody comprising a δ constant region is an IgD antibody, and an antibody comprising an α constant region is an IgA antibody. Further, an antibody comprising a μ constant region is an IgM antibody, and an antibody comprising an ϵ constant region is an IgE antibody. Certain isotypes can be further subdivided into subclasses. For example, IgG antibodies include, but are not limited to, IgG1 (comprising a γ_1 constant region), IgG2 (comprising a γ_2 constant region), IgG3 (comprising a γ_3 constant region), and IgG4 (comprising a γ_4 constant region) antibodies; IgA antibodies include, but are not limited to, IgA1 (comprising an α_1 constant region) and IgA2 (comprising an α_2 constant region) antibodies; and IgM antibodies include, but are not limited to, IgM1 and IgM2.

In some embodiments, a heavy chain constant region comprises one or more mutations (or substitutions), additions, or deletions that confer a desired characteristic on the antibody. A nonlimiting exemplary mutation is the S241P mutation in the IgG4 hinge region (between constant domains C_{H1} and C_{H2}), which alters the IgG4 motif CPSCP to CPPCP, which is similar to the corresponding motif in IgG1. That mutation, in some embodiments, results in a more stable IgG4 antibody. See, e.g., Angal et al., *Mol. Immunol.* 30: 105-108 (1993); Bloom et al., *Prot. Sci.* 6: 407-415 (1997); Schuurman et al., *Mol. Immunol.* 38: 1-8 (2001).

The term "heavy chain" as used herein refers to a polypeptide comprising at least a heavy chain variable region, with or

without a leader sequence. In some embodiments, a heavy chain comprises at least a portion of a heavy chain constant region. The term "full-length heavy chain" as used herein refers to a polypeptide comprising a heavy chain variable region and a heavy chain constant region, with or without a leader sequence.

The term "light chain variable region" as used herein refers to a region comprising light chain CDR1, framework (FR) 2, CDR2, FR3, and CDR3. In some embodiments, a light chain variable region also comprises an FR1 and/or an FR4. In some embodiments, a light chain CDR1 corresponds to Kabat residues 24 to 34; a light chain CDR2 corresponds to Kabat residues 50 to 56; and a light chain CDR3 corresponds to Kabat residues 89 to 97. See, e.g., Kabat Sequences of Proteins of Immunological Interest (1987 and 1991, NIH, Bethesda, Md.); and FIG. 1.

The term "light chain constant region" as used herein refers to a region comprising a light chain constant domain, C_L . Nonlimiting exemplary light chain constant regions include 2, and K.

The term "light chain" as used herein refers to a polypeptide comprising at least a light chain variable region, with or without a leader sequence. In some embodiments, a light chain comprises at least a portion of a light chain constant region. The term "full-length light chain" as used herein refers to a polypeptide comprising a light chain variable region and a light chain constant region, with or without a leader sequence.

A "chimeric antibody" as used herein refers to an antibody comprising at least one variable region from a first species (such as mouse, rat, cynomolgus monkey, etc.) and at least one constant region from a second species (such as human, cynomolgus monkey, etc.). In some embodiments, a chimeric antibody comprises at least one mouse variable region and at least one human constant region. In some embodiments, a chimeric antibody comprises at least one cynomolgus variable region and at least one human constant region. In some embodiments, all of the variable regions of a chimeric antibody are from a first species and all of the constant regions of the chimeric antibody are from a second species.

A "humanized antibody" as used herein refers to an antibody in which at least one amino acid in a framework region of a non-human variable region has been replaced with the corresponding amino acid from a human variable region. In some embodiments, a humanized antibody comprises at least one human constant region or fragment thereof. In some embodiments, a humanized antibody is an Fab, an scFv, a (Fab')₂, etc.

A "CDR-grafted antibody" as used herein refers to a humanized antibody in which the complementarity determining regions (CDRs) of a first (non-human) species have been grafted onto the framework regions (FRs) of a second (human) species.

A "human antibody" as used herein refers to antibodies produced in humans, antibodies produced in non-human animals that comprise human immunoglobulin genes, such as XenoMouse®, and antibodies selected using in vitro methods, such as phage display, wherein the antibody repertoire is based on a human immunoglobulin sequences.

The term "leader sequence" refers to a sequence of amino acid residues located at the N terminus of a polypeptide that facilitates secretion of a polypeptide from a mammalian cell. A leader sequence may be cleaved upon export of the polypeptide from the mammalian cell, forming a mature protein. Leader sequences may be natural or synthetic, and they may be heterologous or homologous to the protein to which they are attached. Exemplary leader sequences include, but

are not limited to, antibody leader sequences, such as, for example, the amino acid sequences of SEQ ID NOs.: 3 and 4, which correspond to human light and heavy chain leader sequences, respectively. Nonlimiting exemplary leader sequences also include leader sequences from heterologous proteins. In some embodiments, an antibody lacks a leader sequence. In some embodiments, an antibody comprises at least one leader sequence, which may be selected from native antibody leader sequences and heterologous leader sequences.

The term "vector" is used to describe a polynucleotide that may be engineered to contain a cloned polynucleotide or polynucleotides that may be propagated in a host cell. A vector may include one or more of the following elements: an origin of replication, one or more regulatory sequences (such as, for example, promoters and/or enhancers) that regulate the expression of the polypeptide of interest, and/or one or more selectable marker genes (such as, for example, antibiotic resistance genes and genes that may be used in colorimetric assays, e.g., β -galactosidase). The term "expression vector" refers to a vector that is used to express a polypeptide of interest in a host cell.

A "host cell" refers to a cell that may be or has been a recipient of a vector or isolated polynucleotide. Host cells may be prokaryotic cells or eukaryotic cells. Exemplary eukaryotic cells include mammalian cells, such as primate or non-primate animal cells; fungal cells, such as yeast; plant cells; and insect cells. Nonlimiting exemplary mammalian cells include, but are not limited to, NSO cells, PER.C6® cells (Crucell), and 293 and CHO cells, and their derivatives, such as 293-6E and DG44 cells, respectively.

The term "isolated" as used herein refers to a molecule that has been separated from at least some of the components with which it is typically found in nature. For example, a polypeptide is referred to as "isolated" when it is separated from at least some of the components of the cell in which it was produced. Where a polypeptide is secreted by a cell after expression, physically separating the supernatant containing the polypeptide from the cell that produced it is considered to be "isolating" the polypeptide. Similarly, a polynucleotide is referred to as "isolated" when it is not part of the larger polynucleotide (such as, for example, genomic DNA or mitochondrial DNA, in the case of a DNA polynucleotide) in which it is typically found in nature, or is separated from at least some of the components of the cell in which it was produced, e.g., in the case of an RNA polynucleotide. Thus, a DNA polynucleotide that is contained in a vector inside a host cell may be referred to as "isolated" so long as that polynucleotide is not found in that vector in nature.

The terms "subject" and "patient" are used interchangeably herein to refer to a human. In some embodiments, methods of treating other mammals, including, but not limited to, rodents, simians, felines, canines, equines, bovines, porcines, ovines, caprines, mammalian laboratory animals, mammalian farm animals, mammalian sport animals, and mammalian pets, are also provided.

The term "rheumatoid arthritis" ("RA") refers to a chronic autoimmune disease characterized primarily by inflammation of the lining (synovium) of the joints, which can lead to joint damage, resulting in chronic pain, loss of function, and disability. Because RA can affect multiple organs of the body, including skin, lungs, and eyes, it is referred to as a systemic illness.

The term "multiple sclerosis" ("MS") refers to the chronic, autoimmune, demyelinating disease of the CNS in which the body generates antibodies and white blood cells against the

cells that produce the myelin sheath. "Demyelination" occurs when the myelin sheath becomes inflamed, injured, and detaches from the nerve fiber.

The term "cancer" refers to a proliferative disorder associated with uncontrolled cell proliferation, unrestrained cell growth, and decreased cell death/apoptosis. Cancer includes, but is not limited to, breast cancer, prostate cancer, lung cancer, kidney cancer, thyroid cancer, esophageal cancer, melanoma, follicular lymphomas, uveal melanoma, brain cancer, head and neck cancer, pulmonary adenocarcinoma, including, but not limited to, colon cancer, cardiac tumors, pancreatic cancer, retinoblastoma, glioblastoma, intestinal cancer, testicular cancer, stomach cancer, neuroblastoma, myxoma, myoma, lymphoma, endothelioma, osteoblastoma, osteoclastoma, osteosarcoma, chondrosarcoma, adenoma, Kaposi's sarcoma, ovarian cancer, leukemia (including acute leukemias (for example, acute lymphocytic leukemia, acute myelocytic leukemia, including myeloblastic, promyelocytic, myelomonocytic, monocytic, and erythroleukemia)) and chronic leukemias (for example, chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia), myelodysplastic syndrome polycythemia vera, lymphomas (for example, Hodgkin's disease, non-Hodgkin's disease), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain diseases, and solid tumors including, but not limited to, sarcomas and carcinomas such as fibrosarcoma, myxosarcoma, liposarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, endometrial cancer, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, and menangioma. The terms "metastasis" and "cancer metastasis" are used interchangeably herein to refer to the ability of a cancer cell to spread to other tissues. For example, "metastasis to bone" refers to the ability of certain types of cancer including, but not limited to, breast, prostate, lung, kidney, thyroid, and melanoma, to metastasize to bone.

The term "osteolytic disorders" is used herein to refer to any condition that is caused by an increase in the activity of osteoclasts, which are cells responsible for bone resorption. The terms "osteolysis" and "osteolytic bone loss" may be used interchangeably to refer to osteoclast-mediated bone resorption or bone loss associated with an osteolytic disorder. Osteolytic disorders may occur in subjects with a predisposition to develop an osteolytic disorder, or they may occur in subjects with a disease that leads to or contributes to an osteolytic disorder by stimulating osteoclast activity. In exemplary embodiments of the present invention, the osteolytic disorder may include osteolytic bone loss and cancer metastasis-induced osteolytic bone loss. In further exemplary embodiments of the present invention, the osteolytic bone disorder includes metabolic bone disease, including endocrinopathies, such as hypercortisolism, hypogonadism, primary or secondary hyperparathyroidism, and hyperthyroidism; dietary deficiency, including rickets, osteomalacia, scurvy, and malnutrition; osteoporosis; drug use, including glucocorticoids (glucocorticoid-induced osteoporosis), heparin, and alcohol; chronic disease, including malabsorption

syndromes; chronic renal failure, including renal osteodystrophy; chronic liver disease, including hepatic osteodystrophy; inherited disease, including osteogenesis imperfecta and homocystinuria; and bone inflammation associated with arthritis, rheumatoid arthritis, psoriatic arthritis, fibrous dysplasia, periodontal disease, and Paget's disease.

The terms "metastasis-induced osteolytic bone loss," and "cancer metastasis-induced osteolytic bone loss," are used interchangeably herein to refer to osteolysis or osteolytic bone loss resulting from cancer cell metastasis to bone. The term "cancer metastasis-induced osteoclast activation" is used herein to refer to the ability of cancer cells that have metastasized to bone to induce the activation of osteoclasts.

The term "tumor" is used herein to refer to a group of cells that exhibit abnormally high levels of proliferation and growth. A tumor may be benign, pre-malignant, or malignant; malignant tumor cells are cancerous. Tumor cells may be solid tumor cells or leukemic tumor cells. The term "tumor growth" is used herein to refer to proliferation or growth by a cell or cells that comprise a tumor that leads to a corresponding increase in the size of the tumor. The term "CSF1R-dependent tumor growth" is used herein to refer to the requirement of a tumor cell or cells for CSF1R-mediated function(s) in order for the tumor cell or cells to proliferate or grow.

"Treatment," as used herein, covers any administration or application of a therapeutic for disease in a mammal, including a human, and includes inhibiting the disease or progression of the disease, inhibiting or slowing the disease or its progression, arresting its development, partially or fully relieving the disease, or curing the disease, for example, by causing regression, or restoring or repairing a lost, missing, or defective function; or stimulating an inefficient process.

The terms "inhibition" or "inhibit" refer to a decrease or cessation of any phenotypic characteristic or to the decrease or cessation in the incidence, degree, or likelihood of that characteristic.

A "pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid, or liquid filler, diluent, encapsulating material, formulation auxiliary, or carrier conventional in the art for use with a therapeutic agent that together comprise a "pharmaceutical composition" for administration to a subject. A pharmaceutically acceptable carrier is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. The pharmaceutically acceptable carrier is appropriate for the formulation employed. For example, if the therapeutic agent is to be administered orally, the carrier may be a gel capsule. If the therapeutic agent is to be administered subcutaneously, the carrier ideally is not irritable to the skin and does not cause injection site reaction.

Anti-CSF1R Antibodies

The present inventors have invented a new set of antibodies directed against CSF1R. Anti-CSF1R antibodies include, but are not limited to, humanized antibodies, chimeric antibodies, mouse antibodies, human antibodies, and antibodies comprising the heavy chain and/or light chain CDRs discussed herein.

Exemplary Humanized Antibodies

In some embodiments, humanized antibodies that bind CSF1R are provided. Humanized antibodies are useful as therapeutic molecules because humanized antibodies reduce or eliminate the human immune response to non-human antibodies (such as the human anti-mouse antibody (HAMA) response), which can result in an immune response to an antibody therapeutic, and decreased effectiveness of the therapeutic.

Nonlimiting exemplary humanized antibodies include Ab1 through Ab16, described herein. Nonlimiting exemplary humanized antibodies also include antibodies comprising a heavy chain variable region of an antibody selected from Ab1 to Ab16 and/or a light chain variable region of an antibody selected from Ab1 to Ab16. Nonlimiting exemplary humanized antibodies include antibodies comprising a heavy chain variable region selected from SEQ ID NOs: 39 to 45 and/or a light chain variable region selected from SEQ ID NOs: 46 to 52. Exemplary humanized antibodies also include, but are not limited to, humanized antibodies comprising heavy chain CDR1, CDR2, and CDR3, and/or light chain CDR1, CDR2, and CDR3 of an antibody selected from 0301, 0302, and 0311.

In some embodiments, a humanized anti-CSF1R antibody comprises heavy chain CDR1, CDR2, and CDR3 and/or a light chain CDR1, CDR2, and CDR3 of an antibody selected from 0301, 0302, and 0311. Nonlimiting exemplary humanized anti-CSF1R antibodies include antibodies comprising sets of heavy chain CDR1, CDR2, and CDR3 selected from: SEQ ID NOs: 15, 16, and 17; SEQ ID NOs: 21, 22, and 23; and SEQ ID NOs: 27, 28, and 29. Nonlimiting exemplary humanized anti-CSF1R antibodies also include antibodies comprising sets of light chain CDR1, CDR2, and CDR3 selected from: SEQ ID NOs: 18, 19, and 20; SEQ ID NOs: 24, 25, and 26; and SEQ ID NOs: 30, 31, and 32.

Nonlimiting exemplary humanized anti-CSF1R antibodies include antibodies comprising the sets of heavy chain CDR1, CDR2, and CDR3, and light chain CDR1, CDR2, and CDR3 in Table 1 (SEQ ID NOs shown; see Table 8 for sequences). Each row of Table 1 shows the heavy chain CDR1, CDR2, and CDR3, and light chain CDR1, CDR2, and CDR3 of an exemplary antibody.

TABLE 1

Heavy chain and light chain CDRs					
Heavy chain			Light chain		
CDR1 SEQ ID	CDR2 SEQ ID	CDR3 SEQ ID	CDR1 SEQ ID	CDR2 SEQ ID	CDR3 SEQ ID
15	16	17	18	19	20
21	22	23	24	25	26
27	28	29	30	31	32

Further Exemplary Humanized Antibodies

In some embodiments, a humanized anti-CSF1R antibody comprises a heavy chain comprising a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45, and wherein the antibody binds CSF1R. In some embodiments, a humanized anti-CSF1R antibody comprises a light chain comprising a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52, wherein the antibody binds CSF1R. In some embodiments, a humanized anti-CSF1R antibody comprises a heavy chain comprising a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45; and a light chain comprising a variable region sequence that is at least 90%, at least 91%, at

least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52; wherein the antibody binds CSF1R.

As used herein, whether a particular polypeptide is, for example, at least 95% identical to an amino acid sequence can be determined using, e.g., a computer program. When determining whether a particular sequence is, for example, 95% identical to a reference sequence, the percentage of identity is calculated over the full length of the reference amino acid sequence.

In some embodiments, a humanized anti-CSF1R antibody comprises at least one of the CDRs discussed herein. That is, in some embodiments, a humanized anti-CSF1R antibody comprises at least one CDR selected from a heavy chain CDR1 discussed herein, a heavy chain CDR2 discussed herein, a heavy chain CDR3 discussed herein, a light chain CDR1 discussed herein, a light chain CDR2 discussed herein, and a light chain CDR3 discussed herein. Further, in some embodiments, a humanized anti-CSF1R antibody comprises at least one mutated CDR based on a CDR discussed herein, wherein the mutated CDR comprises 1, 2, 3, or 4 amino acid substitutions relative to the CDR discussed herein. In some embodiments, one or more of the amino acid substitutions are conservative amino acid substitutions. One skilled in the art can select one or more suitable conservative amino acid substitutions for a particular CDR sequence, wherein the suitable conservative amino acid substitutions are not predicted to significantly alter the binding properties of the antibody comprising the mutated CDR.

Exemplary humanized anti-CSF1R antibodies also include antibodies that compete for binding to CSF1R with an antibody described herein. Thus, in some embodiments, a humanized anti-CSF1R antibody is provided that competes for binding to CSF1R with an antibody selected from Fabs 0301, 0302, and 0311; and bivalent (i.e., having two heavy chains and two light chains) antibody versions of those Fabs.

Exemplary Humanized Antibody Constant Regions

In some embodiments, a humanized antibody described herein comprises one or more human constant regions. In some embodiments, the human heavy chain constant region is of an isotype selected from IgA, IgG, and IgD. In some embodiments, the human light chain constant region is of an isotype selected from κ and λ . In some embodiments, a humanized antibody described herein comprises a human IgG constant region. In some embodiments, a humanized antibody described herein comprises a human IgG4 heavy chain constant region. In some such embodiments, a humanized antibody described herein comprises an S241P mutation in the human IgG4 constant region. In some embodiments, a humanized antibody described herein comprises a human IgG4 constant region and a human κ light chain.

The choice of heavy chain constant region can determine whether or not an antibody will have effector function in vivo. Such effector function, in some embodiments, includes antibody-dependent cell-mediated cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC), and can result in killing of the cell to which the antibody is bound. In some methods of treatment, including methods of treating some cancers, cell killing may be desirable, for example, when the antibody binds to a cell that supports the maintenance or growth of the tumor. Exemplary cells that may support the maintenance or growth of a tumor include, but are not limited to, tumor cells themselves, cells that aid in the recruitment of vasculature to the tumor, and cells that provide ligands, growth factors, or counter-receptors that support or promote tumour growth or tumour survival. In some embodiments,

when effector function is desirable, an anti-CSF1R antibody comprising a human IgG1 heavy chain or a human IgG3 heavy chain is selected.

In some methods of treatment, effector function may not be desirable. For example, in some embodiments, it may be desirable that antibodies used in the treatment of MS and/or RA and/or osteolysis do not have effector function. Thus, in some embodiments, anti-CSF1R antibodies developed for the treatment of cancer may not be suitable for use in treatment of MS and/or RA and/or osteolysis. Accordingly, in some embodiments, an anti-CSF1R antibody that lacks significant effector function is used in treatment of MS and/or RA and/or osteolysis. In some embodiments, an anti-CSF1R antibody for treatment of MS and/or RA and/or osteolysis comprises a human IgG4 or IgG2 heavy chain constant region. In some embodiments, an IgG4 constant region comprises an S241P mutation.

An antibody may be humanized by any method. Nonlimiting exemplary methods of humanization include methods described, e.g., in U.S. Pat. Nos. 5,530,101; 5,585,089; 5,693,761; 5,693,762; 6,180,370; Jones et al., *Nature* 321: 522-525 (1986); Riechmann et al., *Nature* 332: 323-27 (1988); Verhoeyen et al., *Science* 239: 1534-36 (1988); and U.S. Publication No. US 2009/0136500.

As noted above, a humanized antibody is an antibody in which at least one amino acid in a framework region of a non-human variable region has been replaced with the amino acid from the corresponding location in a human framework region. In some embodiments, at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least 10, at least 11, at least 12, at least 15, or at least 20 amino acids in the framework regions of a non-human variable region are replaced with an amino acid from one or more corresponding locations in one or more human framework regions.

In some embodiments, some of the corresponding human amino acids used for substitution are from the framework regions of different human immunoglobulin genes. That is, in some such embodiments, one or more of the non-human amino acids may be replaced with corresponding amino acids from a human framework region of a first human antibody or encoded by a first human immunoglobulin gene, one or more of the non-human amino acids may be replaced with corresponding amino acids from a human framework region of a second human antibody or encoded by a second human immunoglobulin gene, one or more of the non-human amino acids may be replaced with corresponding amino acids from a human framework region of a third human antibody or encoded by a third human immunoglobulin gene, etc. Further, in some embodiments, all of the corresponding human amino acids being used for substitution in a single framework region, for example, FR2, need not be from the same human framework. In some embodiments, however, all of the corresponding human amino acids being used for substitution are from the same human antibody or encoded by the same human immunoglobulin gene.

In some embodiments, an antibody is humanized by replacing one or more entire framework regions with corresponding human framework regions. In some embodiments, a human framework region is selected that has the highest level of homology to the non-human framework region being replaced. In some embodiments, such a humanized antibody is a CDR-grafted antibody.

In some embodiments, following CDR-grafting, one or more framework amino acids are changed back to the corresponding amino acid in a mouse framework region. Such "back mutations" are made, in some embodiments, to retain

one or more mouse framework amino acids that appear to contribute to the structure of one or more of the CDRs and/or that may be involved in antigen contacts and/or appear to be involved in the overall structural integrity of the antibody. In some embodiments, ten or fewer, nine or fewer, eight or fewer, seven or fewer, six or fewer, five or fewer, four or fewer, three or fewer, two or fewer, one, or zero back mutations are made to the framework regions of an antibody following CDR grafting.

In some embodiments, a humanized antibody also comprises a human heavy chain constant region and/or a human light chain constant region.

Exemplary Chimeric Antibodies

In some embodiments, an anti-CSF1R antibody is a chimeric antibody. In some embodiments, an anti-CSF1R antibody comprises at least one non-human variable region and at least one human constant region. In some such embodiments, all of the variable regions of an anti-CSF1R antibody are non-human variable regions, and all of the constant regions of an anti-CSF1R antibody are human constant regions. In some embodiments, one or more variable regions of a chimeric antibody are mouse variable regions. The human constant region of a chimeric antibody need not be of the same isotype as the non-human constant region, if any, it replaces. Chimeric antibodies are discussed, e.g., in U.S. Pat. No. 4,816,567; and Morrison et al. *Proc. Natl. Acad. Sci. USA* 81: 6851-55 (1984).

Nonlimiting exemplary chimeric antibodies include chimeric antibodies comprising the heavy and/or light chain variable regions of an antibody selected from 0301, 0302, and 0311. Additional nonlimiting exemplary chimeric antibodies include chimeric antibodies comprising heavy chain CDR1, CDR2, and CDR3, and/or light chain CDR1, CDR2, and CDR3 of an antibody selected from 0301, 0302, and 0311.

Nonlimiting exemplary chimeric anti-CSF1R antibodies include antibodies comprising the following pairs of heavy and light chain variable regions: SEQ ID NOs: 9 and 10; SEQ ID NOs: 11 and 12; and SEQ ID NOs: 13 and 14.

Nonlimiting exemplary anti-CSF1R antibodies include antibodies comprising a set of heavy chain CDR1, CDR2, and CDR3, and light chain CDR1, CDR2, and CDR3 shown above in Table 1.

Further Exemplary Chimeric Antibodies

In some embodiments, a chimeric anti-CSF1R antibody comprises a heavy chain comprising a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45, wherein the antibody binds CSF1R. In some embodiments, a chimeric anti-CSF1R antibody comprises a light chain comprising a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52, wherein the antibody binds CSF1R. In some embodiments, a chimeric anti-CSF1R antibody comprises a heavy chain comprising a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45; and a light chain comprising a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52; wherein the antibody binds CSF1R.

In some embodiments, a chimeric anti-CSF1R antibody comprises at least one of the CDRs discussed herein. That is, in some embodiments, a chimeric anti-CSF1R antibody comprises at least one CDR selected from a heavy chain CDR1 discussed herein, a heavy chain CDR2 discussed herein, a heavy chain CDR3 discussed herein, a light chain CDR1 discussed herein, a light chain CDR2 discussed herein, and a light chain CDR3 discussed herein. Further, in some embodiments, a chimeric anti-CSF1R antibody comprises at least one mutated CDR based on a CDR discussed herein, wherein the mutated CDR comprises 1, 2, 3, or 4 amino acid substitutions relative to the CDR discussed herein. In some embodiments, one or more of the amino acid substitutions are conservative amino acid substitutions. One skilled in the art can select one or more suitable conservative amino acid substitutions for a particular CDR sequence, wherein the suitable conservative amino acid substitutions are not predicted to significantly alter the binding properties of the antibody comprising the mutated CDR.

Exemplary chimeric anti-CSF1R antibodies also include chimeric antibodies that compete for binding to CSF1R with an antibody described herein. Thus, in some embodiments, a chimeric anti-CSF1R antibody is provided that competes for binding to CSF1R with an antibody selected from Fabs 0301, 0302, and 0311; and bivalent (i.e., having two heavy chains and two light chains) antibody versions of those Fabs.

Exemplary Chimeric Antibody Constant Regions

In some embodiments, a chimeric antibody described herein comprises one or more human constant regions. In some embodiments, the human heavy chain constant region is of an isotype selected from IgA, IgG, and IgD. In some embodiments, the human light chain constant region is of an isotype selected from κ and λ . In some embodiments, a chimeric antibody described herein comprises a human IgG constant region. In some embodiments, a chimeric antibody described herein comprises a human IgG4 heavy chain constant region. In some such embodiments, a chimeric antibody described herein comprises an S241P mutation in the human IgG4 constant region. In some embodiments, a chimeric antibody described herein comprises a human IgG4 constant region and a human κ light chain.

As noted above, whether or not effector function is desirable may depend on the particular method of treatment intended for an antibody. Thus, in some embodiments, when effector function is desirable, a chimeric anti-CSF1R antibody comprising a human IgG1 heavy chain constant region or a human IgG3 heavy chain constant region is selected. In some embodiments, when effector function is not desirable, a chimeric anti-CSF1R antibody comprising a human IgG4 or IgG2 heavy chain constant region is selected.

Exemplary Human Antibodies

Human antibodies can be made by any suitable method. Nonlimiting exemplary methods include making human antibodies in transgenic mice that comprise human immunoglobulin loci. See, e.g., Jakobovits et al., *Proc. Natl. Acad. Sci. USA* 90: 2551-55 (1993); Jakobovits et al., *Nature* 362: 255-8 (1993); Lonberg et al., *Nature* 368: 856-9 (1994); and U.S. Pat. Nos. 5,545,807; 6,713,610; 6,673,986; 6,162,963; 5,545,807; 6,300,129; 6,255,458; 5,877,397; 5,874,299; and 5,545,806.

Nonlimiting exemplary methods also include making human antibodies using phage display libraries. See, e.g., Hoogenboom et al., *J. Mol. Biol.* 227: 381-8 (1992); Marks et al., *J. Mol. Biol.* 222: 581-97 (1991); and PCT Publication No. WO 99/10494.

In some embodiments, a human anti-CSF1R antibody binds to a polypeptide having the sequence of SEQ ID NO: 1.

Exemplary human anti-CSF1R antibodies also include antibodies that compete for binding to CSF1R with an antibody described herein. Thus, in some embodiments, a human anti-CSF1R antibody is provided that competes for binding to CSF1R with an antibody selected from Fabs 0301, 0302, and 0311, and bivalent (i.e., having two heavy chains and two light chains) antibody versions of those Fabs.

In some embodiments, a human anti-CSF1R antibody comprises one or more human constant regions. In some embodiments, the human heavy chain constant region is of an isotype selected from IgA, IgG, and IgD. In some embodiments, the human light chain constant region is of an isotype selected from κ and λ . In some embodiments, a human antibody described herein comprises a human IgG constant region. In some embodiments, a human antibody described herein comprises a human IgG4 heavy chain constant region. In some such embodiments, a human antibody described herein comprises an S241P mutation in the human IgG4 constant region. In some embodiments, a human antibody described herein comprises a human IgG4 constant region and a human κ light chain.

In some embodiments, when effector function is desirable, a human anti-CSF1R antibody comprising a human IgG1 heavy chain constant region or a human IgG3 heavy chain constant region is selected. In some embodiments, when effector function is not desirable, a human anti-CSF1R antibody comprising a human IgG4 or IgG2 heavy chain constant region is selected.

Additional Exemplary Anti-CSF1R Antibodies

Exemplary anti-CSF1R antibodies also include, but are not limited to, mouse, humanized, human, chimeric, and engineered antibodies that comprise, for example, one or more of the CDR sequences described herein. In some embodiments, an anti-CSF1R antibody comprises a heavy chain variable region described herein. In some embodiments, an anti-CSF1R antibody comprises a light chain variable region described herein. In some embodiments, an anti-CSF1R antibody comprises a heavy chain variable region described herein and a light chain variable region described herein. In some embodiments, an anti-CSF1R antibody comprises heavy chain CDR1, CDR2, and CDR3 described herein. In some embodiments, an anti-CSF1R antibody comprises light chain CDR1, CDR2, and CDR3 described herein. In some embodiments, an anti-CSF1R antibody comprises heavy chain CDR1, CDR2, and CDR3 described herein and light chain CDR1, CDR2, and CDR3 described herein.

In some embodiments, an anti-CSF1R antibody comprises a heavy chain variable region of an antibody selected from Fabs 0301, 0302, and 0311. Nonlimiting exemplary anti-CSF1R antibodies also include antibodies comprising a heavy chain variable region of an antibody selected from humanized antibodies Ab1 to Ab16. Nonlimiting exemplary anti-CSF1R antibodies include antibodies comprising a heavy chain variable region comprising a sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45.

In some embodiments, an anti-CSF1R antibody comprises a light chain variable region of an antibody selected from Fabs 0301, 0302, and 311. Nonlimiting exemplary anti-CSF1R antibodies also include antibodies comprising a light chain variable region of an antibody selected from humanized antibodies Ab1 to Ab16. Nonlimiting exemplary anti-CSF1R antibodies include antibodies comprising a light chain variable region comprising a sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52.

In some embodiments, an anti-CSF1R antibody comprises a heavy chain variable region and a light chain variable region of an antibody selected from Fabs 0301, 0302, and 0311.

Nonlimiting exemplary anti-CSF1R antibodies also include antibodies comprising a heavy chain variable region and a light chain variable region of an antibody selected from humanized antibodies Ab1 to Ab16. Nonlimiting exemplary anti-CSF1R antibodies include antibodies comprising the following pairs of heavy and light chain variable regions: SEQ ID NOs: 9 and 10; SEQ ID NOs: 11 and 12; and SEQ ID NOs: 13 and 14; SEQ ID NOs: 39 and 40; SEQ ID NOs: 41 and 42; SEQ ID NOs: 43 and 44; SEQ ID NOs: 45 and 46; SEQ ID NOs: 47 and 48; SEQ ID NOs: 49 and 50; and SEQ ID NOs: 51 and 52. Nonlimiting exemplary anti-CSF1R antibodies also include antibodies comprising the following pairs of heavy and light chains: SEQ ID NOs: 33 and 34; SEQ ID NOs: 35 and 36; and SEQ ID NOs: 37 and 38.

In some embodiments, an anti-CSF1R antibody comprises heavy chain CDR1, CDR2, and CDR3 of an antibody selected from Fabs 0301, 0302, and 0311. Nonlimiting exemplary anti-CSF1R antibodies include antibodies comprising sets of heavy chain CDR1, CDR2, and CDR3 selected from: SEQ ID NOs: 15, 16, and 17; SEQ ID NOs: 21, 22, and 23; and SEQ ID NOs: 27, 28, and 29.

In some embodiments, an anti-CSF1R antibody comprises light chain CDR1, CDR2, and CDR3 of an antibody selected from Fabs 0301, 0302, and 0311. Nonlimiting exemplary anti-CSF1R antibodies include antibodies comprising sets of light chain CDR1, CDR2, and CDR3 selected from: SEQ ID NOs: 18, 19, and 20; SEQ ID NOs: 24, 25, and 26; and SEQ ID NOs: 30, 31, and 32.

In some embodiments, an anti-CSF1R antibody comprises heavy chain CDR1, CDR2, and CDR3, and light chain CDR1, CDR2, and CDR3 of an antibody selected from Fabs 0301, 0302, and 0311.

Nonlimiting exemplary anti-CSF1R antibodies include antibodies comprising the sets of heavy chain CDR1, CDR2, and CDR3, and light chain CDR1, CDR2, and CDR3 shown above in Table 1.

Further Exemplary Antibodies

In some embodiments, an anti-CSF1R antibody comprises a heavy chain comprising a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45, wherein the antibody binds CSF1R. In some embodiments, an anti-CSF1R antibody comprises a light chain comprising a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52, wherein the antibody binds CSF1R. In some embodiments, an anti-CSF1R antibody comprises a heavy chain comprising a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45; and a light chain comprising a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52; wherein the antibody binds CSF1R.

In some embodiments, an anti-CSF1R antibody comprises at least one of the CDRs discussed herein. That is, in some embodiments, an anti-CSF1R antibody comprises at least one CDR selected from a heavy chain CDR1 discussed herein, a heavy chain CDR2 discussed herein, a heavy chain CDR3 discussed herein, a light chain CDR1 discussed herein, a light chain CDR2 discussed herein, and a light chain CDR3 dis-

cussed herein. Further, in some embodiments, an anti-CSF1R antibody comprises at least one mutated CDR based on a CDR discussed herein, wherein the mutated CDR comprises 1, 2, 3, or 4 amino acid substitutions relative to the CDR discussed herein. In some embodiments, one or more of the amino acid substitutions are conservative amino acid substitutions. One skilled in the art can select one or more suitable conservative amino acid substitutions for a particular CDR sequence, wherein the suitable conservative amino acid substitutions are not predicted to significantly alter the binding properties of the antibody comprising the mutated CDR.

Exemplary anti-CSF1R antibodies also include antibodies that compete for binding to CSF1R with an antibody described herein. Thus, in some embodiments, an anti-CSF1R antibody is provided that competes for binding to CSF1R with an antibody selected from Fabs 0301, 0302, and 0311, and bivalent (i.e., having two heavy chains and two light chains) antibody versions of those Fabs.

Exemplary Antibody Constant Regions

In some embodiments, an antibody described herein comprises one or more human constant regions. In some embodiments, the human heavy chain constant region is of an isotype selected from IgA, IgG, and IgD. In some embodiments, the human light chain constant region is of an isotype selected from κ and λ . In some embodiments, an antibody described herein comprises a human IgG constant region. In some embodiments, an antibody described herein comprises a human IgG4 heavy chain constant region. In some such embodiments, an antibody described herein comprises an S241P mutation in the human IgG4 constant region. In some

embodiments, an antibody described herein comprises a human IgG4 constant region and a human κ light chain. As noted above, whether or not effector function is desirable may depend on the particular method of treatment intended for an antibody. Thus, in some embodiments, when effector function is desirable, an anti-CSF1R antibody comprising a human IgG1 heavy chain constant region or a human IgG3 heavy chain constant region is selected. In some embodiments, when effector function is not desirable, an anti-CSF1R antibody comprising a human IgG4 or IgG2 heavy chain constant region is selected.

Exemplary Anti-CSF1R Heavy Chain Variable Regions

In some embodiments, anti-CSF1R antibody heavy chain variable regions are provided. In some embodiments, an anti-CSF1R antibody heavy chain variable region is a mouse variable region, a human variable region, or a humanized variable region.

An anti-CSF1R antibody heavy chain variable region comprises a heavy chain CDR1, FR2, CDR2, FR3, and CDR3. In some embodiments, an anti-CSF1R antibody heavy chain variable region further comprises a heavy chain FR1 and/or FR4. Nonlimiting exemplary heavy chain variable regions include, but are not limited to, heavy chain variable regions having an amino acid sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45.

In some embodiments, an anti-CSF1R antibody heavy chain variable region comprises a CDR1 comprising a sequence selected from SEQ ID NOs: 15, 21, and 27.

In some embodiments, an anti-CSF1R antibody heavy chain variable region comprises a CDR2 comprising a sequence selected from SEQ ID NOs: 16, 22, and 28.

In some embodiments, an anti-CSF1R antibody heavy chain variable region comprises a CDR3 comprising a sequence selected from SEQ ID NOs: 17, 23, and 29.

Nonlimiting exemplary heavy chain variable regions include, but are not limited to, heavy chain variable regions comprising sets of CDR1, CDR2, and CDR3 selected from:

SEQ ID NOs: 15, 16, and 17; SEQ ID NOs: 21, 22, and 23; and SEQ ID NOs: 27, 28, and 29.

In some embodiments, an anti-CSF1R antibody heavy chain comprises a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45, wherein the heavy chain, together with a light chain, is capable of forming an antibody that binds CSF1R.

In some embodiments, an anti-CSF1R antibody heavy chain comprises at least one of the CDRs discussed herein. That is, in some embodiments, an anti-CSF1R antibody heavy chain comprises at least one CDR selected from a heavy chain CDR1 discussed herein, a heavy chain CDR2 discussed herein, and a heavy chain CDR3 discussed herein. Further, in some embodiments, an anti-CSF1R antibody heavy chain comprises at least one mutated CDR based on a CDR discussed herein, wherein the mutated CDR comprises 1, 2, 3, or 4 amino acid substitutions relative to the CDR discussed herein. In some embodiments, one or more of the amino acid substitutions are conservative amino acid substitutions. One skilled in the art can select one or more suitable conservative amino acid substitutions for a particular CDR sequence, wherein the suitable conservative amino acid substitutions are not predicted to significantly alter the binding properties of the heavy chain comprising the mutated CDR.

In some embodiments, a heavy chain comprises a heavy chain constant region. In some embodiments, a heavy chain comprises a human heavy chain constant region. In some embodiments, the human heavy chain constant region is of an isotype selected from IgA, IgG, and IgD. In some embodiments, the human heavy chain constant region is an IgG constant region. In some embodiments, a heavy chain comprises a human IgG4 heavy chain constant region. In some such embodiments, the human IgG4 heavy chain constant region comprises an S241P mutation.

In some embodiments, when effector function is desirable, a heavy chain comprises a human IgG1 or IgG3 heavy chain constant region. In some embodiments, when effector function is less desirable, a heavy chain comprises a human IgG4 or IgG2 heavy chain constant region.

Exemplary Anti-CSF1R Light Chain Variable Regions

In some embodiments, anti-CSF1R antibody light chain variable regions are provided. In some embodiments, an anti-CSF1R antibody light chain variable region is a mouse variable region, a human variable region, or a humanized variable region.

An anti-CSF1R antibody light chain variable region comprises a light chain CDR1, FR2, CDR2, FR3, and CDR3. In some embodiments, an anti-CSF1R antibody light chain variable region further comprises a light chain FR1 and/or FR4. Nonlimiting exemplary light chain variable regions include light chain variable regions having an amino acid sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52.

In some embodiments, an anti-CSF1R antibody light chain variable region comprises a CDR1 comprising a sequence selected from SEQ ID NOs: 18, 24 and 30.

In some embodiments, an anti-CSF1R antibody light chain variable region comprises a CDR2 comprising a sequence selected from SEQ ID NOs: 19, 25, and 31.

In some embodiments, an anti-CSF1R antibody light chain variable region comprises a CDR3 comprising a sequence selected from SEQ ID NOs: 20, 26, and 32.

Nonlimiting exemplary light chain variable regions include, but are not limited to, light chain variable regions comprising sets of CDR1, CDR2, and CDR3 selected from:

SEQ ID NOs: 18, 19, and 20; SEQ ID NOs: 24, 25, and 26; and SEQ ID NOs: 30, 31, and 32.

In some embodiments, an anti-CSF1R antibody light chain comprises a variable region sequence that is at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52, wherein the light chain, together with a heavy chain, is capable of forming an antibody that binds CSF1R.

In some embodiments, an anti-CSF1R antibody light chain comprises at least one of the CDRs discussed herein. That is, in some embodiments, an anti-CSF1R antibody light chain comprises at least one CDR selected from a light chain CDR1 discussed herein, a light chain CDR2 discussed herein, and a light chain CDR3 discussed herein. Further, in some embodiments, an anti-CSF1R antibody light chain comprises at least one mutated CDR based on a CDR discussed herein, wherein the mutated CDR comprises 1, 2, 3, or 4 amino acid substitutions relative to the CDR discussed herein. In some embodiments, one or more of the amino acid substitutions are conservative amino acid substitutions. One skilled in the art can select one or more suitable conservative amino acid substitutions for a particular CDR sequence, wherein the suitable conservative amino acid substitutions are not predicted to significantly alter the binding properties of the light chain comprising the mutated CDR.

In some embodiments, a light chain comprises a human light chain constant region. In some embodiments, a human light chain constant region is selected from a human κ and a human λ , light chain constant region.

Exemplary Additional CSF1R Binding Molecules

In some embodiments, additional molecules that bind CSF1R are provided. Such molecules include, but are not limited to, non-canonical scaffolds, such as anti-calins, adnectins, ankyrin repeats, etc. See, e.g., Hosse et al., *Prot. Sci.* 15:14 (2006); Fiedler, M. and Skerra, A., "Non-Antibody Scaffolds," pp. 467-499 in *Handbook of Therapeutic Antibodies*, Dubel, S., ed., Wiley-VCH, Weinheim, Germany, 2007.

Exemplary Properties of anti-CSF1R antibodies

In some embodiments, an antibody having a structure described above binds to the CSF1R with a binding affinity (K_D) of less than 1 nM, blocks binding of CSF1 and/or IL34 to CSF1R, and inhibits CSF1R phosphorylation induced by CSF1 and/or IL34.

In some embodiments, an anti-CSF1R antibody binds to the extracellular domain of CSF1R (CSF1R-ECD). In some embodiments, an anti-CSF1R antibody has a binding affinity (K_D) for CSF1R of less than 1 nM, less than 0.5 nM, less than 0.1 nM, or less than 0.05 nM. In some embodiments, an anti-CSF1R antibody has a K_D of between 0.01 and 1 nM, between 0.01 and 0.5 nM, between 0.01 and 0.1 nM, between 0.01 and 0.05 nM, or between 0.02 and 0.05 nM.

In some embodiments, an anti-CSF1R antibody blocks ligand binding to CSF1R. In some embodiments, an anti-CSF1R antibody blocks binding of CSF1 to CSF1R. In some embodiments, an anti-CSF1R antibody blocks binding of IL34 to CSF1R. In some embodiments, an anti-CSF1R antibody blocks binding of both CSF1 and IL34 to CSF1R. In some embodiments, an antibody that blocks ligand binding binds to the extracellular domain of CSF1R. An antibody is considered to "block ligand binding to CSF1R" when it reduces the amount of detectable binding of a ligand to CSF1R by at least 50%, using the assay described in Example 7. In some embodiments, an antibody reduces the amount of detectable binding of a ligand to CSF1R by at least 60%, at least 70%, at least 80%, or at least 90%, using the assay

described in Example 7. In some such embodiments, the antibody is said to block ligand binding by at least 50%, at least 60%, at least 70%, etc.

In some embodiments, an anti-CSF1R antibody inhibits ligand-induced CSF1R phosphorylation. In some embodiments, an anti-CSF1R antibody inhibits CSF1-induced CSF1R phosphorylation. In some embodiments, an anti-CSF1R antibody inhibits IL34-induced CSF1R phosphorylation. In some embodiments, an anti-CSF1R antibody inhibits both CSF1-induced and IL34-induced CSF1R phosphorylation. An antibody is considered to "inhibit ligand-induced CSF1R phosphorylation" when it reduces the amount of detectable ligand-induced CSF1R phosphorylation by at least 50%, using the assay described in Example 6. In some embodiments, an antibody reduces the amount of detectable ligand-induced CSF1R phosphorylation by at least 60%, at least 70%, at least 80%, or at least 90%, using the assay described in Example 6. In some such embodiments, the antibody is said to inhibit ligand-induced CSF1R phosphorylation by at least 50%, at least 60%, at least 70%, etc.

In some embodiments, an antibody inhibits monocyte proliferation and/or survival responses in the presence of CSF1 and/or IL34. An antibody is considered to "inhibit monocyte proliferation and/or survival responses" when it reduces the amount of monocyte proliferation and/or survival responses in the presence of CSF1 and/or IL34 by at least 50%, using the assay described in Example 10. In some embodiments, an antibody reduces the amount of monocyte proliferation and/or survival responses in the presence of CSF1 and/or IL34 by at least 60%, at least 70%, at least 80%, or at least 90%, using the assay described in Example 10. In some such embodiments, the antibody is said to inhibit monocyte proliferation and/or survival responses by at least 50%, at least 60%, at least 70%, etc.

Exemplary Antibody Conjugates

In some embodiments, an anti-CSF1R antibody is conjugated to a label and/or a cytotoxic agent. As used herein, a label is a moiety that facilitates detection of the antibody and/or facilitates detection of a molecule to which the antibody binds. Nonlimiting exemplary labels include, but are not limited to, radioisotopes, fluorescent groups, enzymatic groups, chemiluminescent groups, biotin, epitope tags, metal-binding tags, etc. One skilled in the art can select a suitable label according to the intended application.

As used herein, a cytotoxic agent is a moiety that reduces the proliferative capacity of one or more cells. A cell has reduced proliferative capacity when the cell becomes less able to proliferate, for example, because the cell undergoes apoptosis or otherwise dies, the cell fails to proceed through the cell cycle and/or fails to divide, the cell differentiates, etc. Nonlimiting exemplary cytotoxic agents include, but are not limited to, radioisotopes, toxins, and chemotherapeutic agents. One skilled in the art can select a suitable cytotoxic agent according to the intended application.

In some embodiments, a label and/or a cytotoxic agent is conjugated to an antibody using chemical methods in vitro. Nonlimiting exemplary chemical methods of conjugation are known in the art, and include services, methods and/or reagents commercially available from, e.g., Thermo Scientific Life Science Research Products (formerly Pierce; Rockford, Ill.), Prozyme (Hayward, Calif.), SACRI Antibody Services (Calgary, Canada), AbD Serotec (Raleigh, N.C.), etc. In some embodiments, when a label and/or cytotoxic agent is a polypeptide, the label and/or cytotoxic agent can be expressed from the same expression vector with at least one antibody chain to produce a polypeptide comprising the label

and/or cytotoxic agent fused to an antibody chain. One skilled in the art can select a suitable method for conjugating a label and/or cytotoxic agent to an antibody according to the intended application.

Exemplary Leader Sequences

In order for some secreted proteins to express and secrete in large quantities, a leader sequence from a heterologous protein may be desirable. In some embodiments, a leader sequence is selected from SEQ ID NOs: 3 and 4, which are light chain and heavy chain leader sequences, respectively. In some embodiments, employing heterologous leader sequences may be advantageous in that a resulting mature polypeptide may remain unaltered as the leader sequence is removed in the ER during the secretion process. The addition of a heterologous leader sequence may be required to express and secrete some proteins.

Certain exemplary leader sequence sequences are described, e.g., in the online Leader sequence Database maintained by the Department of Biochemistry, National University of Singapore. See Choo et al., *BMC Bioinformatics*, 6: 249 (2005); and PCT Publication No. WO 2006/081430.

Nucleic Acid Molecules Encoding Anti-CSF1R Antibodies

Nucleic acid molecules comprising polynucleotides that encode one or more chains of anti-CSF1R antibodies are provided. In some embodiments, a nucleic acid molecule comprises a polynucleotide that encodes a heavy chain or a light chain of an anti-CSF1R antibody. In some embodiments, a nucleic acid molecule comprises both a polynucleotide that encodes a heavy chain and a polynucleotide that encodes a light chain, of an anti-CSF1R antibody. In some embodiments, a first nucleic acid molecule comprises a first polynucleotide that encodes a heavy chain and a second nucleic acid molecule comprises a second polynucleotide that encodes a light chain.

In some such embodiments, the heavy chain and the light chain are expressed from one nucleic acid molecule, or from two separate nucleic acid molecules, as two separate polypeptides. In some embodiments, such as when an antibody is an scFv, a single polynucleotide encodes a single polypeptide comprising both a heavy chain and a light chain linked together.

In some embodiments, a polynucleotide encoding a heavy chain or light chain of an anti-CSF1R antibody comprises a nucleotide sequence that encodes a leader sequence, which, when translated, is located at the N terminus of the heavy chain or light chain. As discussed above, the leader sequence may be the native heavy or light chain leader sequence, or may be another heterologous leader sequence.

Nucleic acid molecules may be constructed using recombinant DNA techniques conventional in the art. In some embodiments, a nucleic acid molecule is an expression vector that is suitable for expression in a selected host cell.

Anti-CSF1R Antibody Expression and Production Vectors

Vectors comprising polynucleotides that encode anti-CSF1R heavy chains and/or anti-CSF1R light chains are provided. Vectors comprising polynucleotides that encode anti-CSF1R heavy chains and/or anti-CSF1R light chains are also provided. Such vectors include, but are not limited to, DNA vectors, phage vectors, viral vectors, retroviral vectors, etc. In some embodiments, a vector comprises a first polynucleotide sequence encoding a heavy chain and a second polynucleotide sequence encoding a light chain. In some embodiments, the heavy chain and light chain are expressed from the vector as two separate polypeptides. In some embodiments, the

heavy chain and light chain are expressed as part of a single polypeptide, such as, for example, when the antibody is an scFv.

In some embodiments, a first vector comprises a polynucleotide that encodes a heavy chain and a second vector comprises a polynucleotide that encodes a light chain. In some embodiments, the first vector and second vector are transfected into host cells in similar amounts (such as similar molar amounts or similar mass amounts). In some embodiments, a mole- or mass-ratio of between 5:1 and 1:5 of the first vector and the second vector is transfected into host cells. In some embodiments, a mass ratio of between 1:1 and 1:5 for the vector encoding the heavy chain and the vector encoding the light chain is used. In some embodiments, a mass ratio of 1:2 for the vector encoding the heavy chain and the vector encoding the light chain is used.

In some embodiments, a vector is selected that is optimized for expression of polypeptides in CHO or CHO-derived cells, or in NSO cells. Exemplary such vectors are described, e.g., in Running Deer et al., *Biotechnol. Prog.* 20:880-889 (2004).

In some embodiments, a vector is chosen for in vivo expression of anti-CSF1R heavy chains and/or anti-CSF1R light chains in animals, including humans. In some such embodiments, expression of the polypeptide is under the control of a promoter that functions in a tissue-specific manner. For example, liver-specific promoters are described, e.g., in PCT Publication No. WO 2006/076288.

Host Cells

In various embodiments, anti-CSF1R heavy chains and/or anti-CSF1R light chains may be expressed in prokaryotic cells, such as bacterial cells; or in eukaryotic cells, such as fungal cells (such as yeast), plant cells, insect cells, and mammalian cells. Such expression may be carried out, for example, according to procedures known in the art. Exemplary eukaryotic cells that may be used to express polypeptides include, but are not limited to, COS cells, including COS 7 cells; 293 cells, including 293-6E cells; CHO cells, including CHO-S and DG44 cells; PER.C6® cells (Crucell); and NSO cells. In some embodiments, anti-CSF1R heavy chains and/or anti-CSF1R light chains may be expressed in yeast. See, e.g., U.S. Publication No. US 2006/0270045 A1. In some embodiments, a particular eukaryotic host cell is selected based on its ability to make desired post-translational modifications to the anti-CSF1R heavy chains and/or anti-CSF1R light chains. For example, in some embodiments, CHO cells produce polypeptides that have a higher level of sialylation than the same polypeptide produced in 293 cells.

Introduction of one or more nucleic acids into a desired host cell may be accomplished by any method, including but not limited to, calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, etc. Nonlimiting exemplary methods are described, e.g., in Sambrook et al., *Molecular Cloning, A Laboratory Manual*, 3rd ed. Cold Spring Harbor Laboratory Press (2001). Nucleic acids may be transiently or stably transfected in the desired host cells, according to any suitable method.

In some embodiments, one or more polypeptides may be produced in vivo in an animal that has been engineered or transfected with one or more nucleic acid molecules encoding the polypeptides, according to any suitable method.

Purification of Anti-CSF1R Antibodies

Anti-CSF1R antibodies may be purified by any suitable method. Such methods include, but are not limited to, the use of affinity matrices or hydrophobic interaction chromatography. Suitable affinity ligands include the CSF1R ECD and ligands that bind antibody constant regions. For example, a

Protein A, Protein G, Protein A/G, or an antibody affinity column may be used to bind the constant region and to purify an anti-CSF1R antibody. Hydrophobic interactive chromatography, for example, a butyl or phenyl column, may also be suitable for purifying some polypeptides. Many methods of purifying polypeptides are known in the art.

Cell-Free Production of Anti-CSF1R Antibodies

In some embodiments, an anti-CSF1R antibody is produced in a cell-free system. Nonlimiting exemplary cell-free systems are described, e.g., in Sitaraman et al., *Methods Mol. Biol.* 498: 229-44 (2009); Spirin, *Trends Biotechnol.* 22: 538-45 (2004); Endo et al., *Biotechnol. Adv.* 21: 695-713 (2003). Therapeutic Compositions and Methods

Methods of Treating Diseases Using Anti-CSF1R Antibodies

Antibodies of the invention, and compositions comprising antibodies of the invention, are provided for use in methods of treatment for humans or animals. Methods of treating disease comprising administering anti-CSF1R antibodies are also provided. Nonlimiting exemplary diseases that can be treated with anti-CSF1R antibodies include, but are not limited to, RA, MS, cancer, metastasis-induced osteolytic bone loss, osteolytic disorders, and hypercalcemia-induced bone loss.

In some embodiments, methods of treating inflammatory conditions comprising administering an anti-CSF1R antibody are provided. In some embodiments, an inflammatory condition is selected from: psoriasis, SLE (lupus), COPD, atopic dermatitis, and atherosclerosis, macrophage activation syndrome, and histiocytosis X.

In some embodiments, methods of treating an inflammatory condition comprising administering an anti-CSF1R antibody are provided, wherein the inflammatory condition is selected from: proliferative vascular disease, acute respiratory distress syndrome, cytokine-mediated toxicity, interleukin-2 toxicity, appendicitis, peptic, gastric and duodenal ulcers, peritonitis, pancreatitis, ulcerative, pseudomembranous, acute and ischemic colitis, diverticulitis, epiglottitis, achalasia, cholangitis, cholecystitis, hepatitis, inflammatory bowel disease, Crohn's disease, enteritis, Whipple's disease, asthma, allergy, anaphylactic shock, immune complex disease, organ ischemia, reperfusion injury, organ necrosis, hay fever, sepsis, septicemia, endotoxic shock, cachexia, hyperpyrexia, eosinophilic granuloma, granulomatosis, sarcoidosis, septic abortion, epididymitis, vaginitis, prostatitis, urethritis, bronchitis, emphysema, rhinitis, cystic fibrosis, pneumonitis, alveolitis, bronchiolitis, pharyngitis, pleurisy, sinusitis, influenza, respiratory syncytial virus infection, herpes infection, HIV infection, hepatitis B virus infection, hepatitis C virus infection, disseminated bacteremia, Dengue fever, candidiasis, malaria, filariasis, amebiasis, hydatid cysts, burns, dermatitis, dermatomyositis, sunburn, urticaria, warts, wheals, vasculitis, angiitis, endocarditis, arteritis, atherosclerosis, thrombophlebitis, pericarditis, myocarditis, myocardial ischemia, periarteritis nodosa, rheumatic fever, Alzheimer's disease, celiac disease, congestive heart failure, meningitis, encephalitis, cerebral infarction, cerebral embolism, Guillain-Barre syndrome, neuritis, neuralgia, spinal cord injury, paralysis, uveitis, arthritides, arthralgias, osteomyelitis, fasciitis, Paget's disease, gout, periodontal disease, synovitis, myasthenia gravis, thyroiditis, systemic lupus erythematosus, Goodpasture's syndrome, Behcet's syndrome, allograft rejection, graft-versus-host disease, ankylosing spondylitis, Berger's disease, type I diabetes, type 2 diabetes, Berger's disease, Retier's syndrome, and Hodgkins disease, or in treating inflammation associated with these conditions.

In some embodiments, methods of treating cancer comprising administering an anti-CSF1R antibody are provided. In some embodiments, the cancer is a CSF1-secreting cancer. In some embodiments, the cancer is one or more cancers selected from breast cancer, prostate cancer, endometrial cancer, bladder cancer, kidney cancer, esophageal cancer, squamous cell carcinoma, uveal melanoma, follicular lymphoma, renal cell carcinoma, cervical cancer, and ovarian cancer. In some embodiments, an anti-CSF1R antibody is useful for treating one or more cancers selected from lung cancer, colorectal cancer, brain cancer, pancreatic cancer, head and neck cancer, liver cancer, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, melanoma, astrocytoma, stomach cancer, and pulmonary adenocarcinoma.

Routes of Administration and Carriers

In various embodiments, anti-CSF1R antibodies may be administered in vivo by various routes, including, but not limited to, oral, intra-arterial, parenteral, intranasal, intramuscular, intracardiac, intraventricular, intratracheal, buccal, rectal, intraperitoneal, intradermal, topical, transdermal, and intrathecal, or otherwise by implantation or inhalation. The subject compositions may be formulated into preparations in solid, semi-solid, liquid, or gaseous forms; including, but not limited to, tablets, capsules, powders, granules, ointments, solutions, suppositories, enemas, injections, inhalants, and aerosols. A nucleic acid molecule encoding an anti-CSF1R antibody may be coated onto gold microparticles and delivered intradermally by a particle bombardment device, or "gene gun," as described in the literature (see, e.g., Tang et al., *Nature* 356:152-154 (1992)). The appropriate formulation and route of administration may be selected according to the intended application.

In various embodiments, compositions comprising anti-CSF1R antibodies are provided in formulations with a wide variety of pharmaceutically acceptable carriers (see, e.g., Gennaro, *Remington: The Science and Practice of Pharmacy with Facts and Comparisons: Drugfacts Plus*, 20th ed. (2003); Ansel et al., *Pharmaceutical Dosage Forms and Drug Delivery Systems*, 7th ed., Lippencott Williams and Wilkins (2004); Kibbe et al., *Handbook of Pharmaceutical Excipients*, 3rd ed., Pharmaceutical Press (2000)). Various pharmaceutically acceptable carriers, which include vehicles, adjuvants, and diluents, are available. Moreover, various pharmaceutically acceptable auxiliary substances, such as pH adjusting and buffering agents, tonicity adjusting agents, stabilizers, wetting agents and the like, are also available. Non-limiting exemplary carriers include saline, buffered saline, dextrose, water, glycerol, ethanol, and combinations thereof.

In various embodiments, compositions comprising anti-CSF1R antibodies may be formulated for injection, including subcutaneous administration, by dissolving, suspending, or emulsifying them in an aqueous or nonaqueous solvent, such as vegetable or other oils, synthetic aliphatic acid glycerides, esters of higher aliphatic acids, or propylene glycol; and if desired, with conventional additives such as solubilizers, isotonic agents, suspending agents, emulsifying agents, stabilizers and preservatives. In various embodiments, the compositions may be formulated for inhalation, for example, using pressurized acceptable propellants such as dichlorodifluoromethane, propane, nitrogen, and the like. The compositions may also be formulated, in various embodiments, into sustained release microcapsules, such as with biodegradable or non-biodegradable polymers. A non-limiting exemplary biodegradable formulation includes poly lactic acid-glycolic acid polymer. A non-limiting exemplary non-biodegradable

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formulation includes a polyglycerin fatty acid ester. Certain methods of making such formulations are described, for example, in EP 1 125 584 A1.

Pharmaceutical packs and kits comprising one or more containers, each containing one or more doses of an anti-CSF1R antibody are also provided. In some embodiments, a unit dosage is provided wherein the unit dosage contains a predetermined amount of a composition comprising an anti-CSF1R antibody, with or without one or more additional agents. In some embodiments, such a unit dosage is supplied in single-use prefilled syringe for injection. In various embodiments, the composition contained in the unit dosage may comprise saline, sucrose, or the like; a buffer, such as phosphate, or the like; and/or be formulated within a stable and effective pH range. Alternatively, in some embodiments, the composition may be provided as a lyophilized powder that may be reconstituted upon addition of an appropriate liquid, for example, sterile water. In some embodiments, the composition comprises one or more substances that inhibit protein aggregation, including, but not limited to, sucrose and arginine. In some embodiments, a composition of the invention comprises heparin and/or a proteoglycan.

Pharmaceutical compositions are administered in an amount effective for treatment or prophylaxis of the specific indication. The therapeutically effective amount is typically dependent on the weight of the subject being treated, his or her physical or health condition, the extensiveness of the condition to be treated, or the age of the subject being treated. In general, anti-CSF1R antibodies may be administered in an amount in the range of about 10 µg/kg body weight to about 100 mg/kg body weight per dose. In some embodiments, anti-CSF1R antibodies may be administered in an amount in the range of about 50 µg/kg body weight to about 5 mg/kg body weight per dose. In some embodiments, anti-CSF1R antibodies may be administered in an amount in the range of about 100 µg/kg body weight to about 10 mg/kg body weight per dose. In some embodiments, anti-CSF1R antibodies may be administered in an amount in the range of about 100 µg/kg body weight to about 20 mg/kg body weight per dose. In some embodiments, anti-CSF1R antibodies may be administered in an amount in the range of about 0.5 mg/kg body weight to about 20 mg/kg body weight per dose.

The anti-CSF1R antibody compositions may be administered as needed to subjects. Determination of the frequency of administration may be made by persons skilled in the art, such as an attending physician based on considerations of the condition being treated, age of the subject being treated, severity of the condition being treated, general state of health of the subject being treated and the like. In some embodiments, an effective dose of an anti-CSF1R antibody is administered to a subject one or more times. In various embodiments, an effective dose of an anti-CSF1R antibody is administered to the subject once a month, more than once a month, such as, for example, every two months or every three months. In other embodiments, an effective dose of an anti-CSF1R antibody is administered less than once a month, such as, for example, every two weeks or every week. An effective dose of an anti-CSF1R antibody is administered to the subject at least once. In some embodiments, the effective dose of an anti-CSF1R antibody may be administered multiple times, including for periods of at least a month, at least six months, or at least a year.

Combination Therapy

Anti-CSF1R antibodies may be administered alone or with other modes of treatment. They may be provided before, substantially contemporaneous with, or after other modes of treatment, for example, surgery, chemotherapy, radiation

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therapy, or the administration of a biologic, such as another therapeutic antibody. For treatment of rheumatoid arthritis, anti-CSF1R antibodies may be administered with other therapeutic agents, for example, methotrexate, anti-TNF agents such as Remicade, Humira, Simponi, and Enbrel; glucocorticoids such as prednisone; Leflunomide; Azathioprine; JAK inhibitors such as CP 590690; SYK inhibitors such as R788; anti-IL-6 antibodies; anti-IL-6R antibodies; anti-CD-20 antibodies; anti-CD19 antibodies; anti-GM-CSF antibodies; and anti-GM-CSF—R antibodies. For treatment of multiple sclerosis, anti-CSF1R antibodies may be administered with other therapeutic agents, for example, interferon alpha; interferon beta; prednisone; anti-alpha4 integrin antibodies such as Tysabri; anti-CD₂O antibodies such as Rituxan; FTY720 (Fingolimod); and Cladribine (Leustatin).

EXAMPLES

The examples discussed below are intended to be purely exemplary of the invention and should not be considered to limit the invention in any way. The examples are not intended to represent that the experiments below are all or the only experiments performed. Efforts have been made to ensure accuracy with respect to numbers used (for example, amounts, temperature, etc.) but some experimental errors and deviations should be accounted for. Unless indicated otherwise, parts are parts by weight, molecular weight is weight average molecular weight, temperature is in degrees Centigrade, and pressure is at or near atmospheric.

Example 1

Selection of Fabs that Bind CSF1R Extracellular Domain (ECD)

Mice were immunized with a human CSF1R extracellular domain Fc fusion, hCSF1R ECD.506-Fc (SEQ ID NO: 6). Splens from immunized mice were isolated, and a Fab phage display library was created from the splenocytes. Fab-expressing phage were selected for binding to human CSF1R ECD. Fabs from positive-binding phage were expressed and purified from bacteria. A total of 1056 Fab clones were selected for further analysis.

Fabs were screened for the ability to bind human CSF1R ECD, block binding of human CSF1 to human CSF1R ECD, and block binding of human IL34 to human CSF1R ECD. Sequence analysis and clustering of the Fabs that were selected from that screen was then performed and certain unique Fabs were selected.

The unique Fabs were further analyzed for the ability to bind human CSF1R ECD, the ability to bind cynomolgus CSF1R ECD, and the ability to bind mouse CSF1R ECD. The Fabs were also analyzed for the ability to block human CSF1 binding to human CSF1R ECD and the ability to block human IL34 binding to human CSF1R ECD, and the ability to inhibit ligand-induced CSF1R phosphorylation in the presence of CSF1 or IL34. (Data not shown.)

Example 2

Reformatting of Anti-CSF1R Fabs to Make Chimeric Antibodies

Following the Fab characterization, eleven of the Fabs were selected for reformatting to chimeric antibodies. Each Fab was reformatted to a chimeric antibody comprising a human IgG4 heavy chain constant region with the S241P

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mutation, and a human κ light chain constant region. Briefly, Fab VH regions cloned into and expressed from vector pTT5 (Biotechnology Research Institute, Montreal, Canada; and National Research Research Council of Canada, Ottawa, Canada) modified to contain a mouse IgH leader sequence (SEQ ID NO: 4) and a human IgG4 heavy chain constant region with the S241P mutation (SEQ ID NO: 94). Fab VL regions were cloned into and expressed from vector pTT5 modified to contain a mouse Igic leader sequence (SEQ ID NO: 3) and a human Igic light chain constant region (SEQ ID NO: 95). Fab V regions were inserted in such a way as not to introduce non-antibody derived amino acid sequences into the final proteins.

Example 3

Expression and Characterization of Chimeric Antibodies

The chimeric antibodies were transiently expressed and purified substantially as described below in Example 5.

The 11 chimeric antibodies were assayed for binding to human, cynomolgus, and mouse CSF1R ECD. The chimeric antibodies were also assayed for the ability to block binding of human CSF1 to human CSF1R ECD, the ability to block binding of human IL34 to human CSF1R ECD, the ability to block binding of human CSF1 to cynomolgus CSF1R ECD, and the ability to inhibit ligand-induced CSF1R phosphorylation in the presence of CSF1 or IL34. The chimeric antibodies were further assayed for binding to CSF1R on the surface of cells. Finally, the chimeric antibodies were assayed to confirm that they do not induce CSF1R phosphorylation in the absence of ligand. (Data not shown.)

Example 4

Humanization of Anti-CSF1R Antibodies

From the analyses described above, chimeric anti-CSF1R antibodies 0301, 0302, and 0311 were selected for humanization. The antibodies were humanized by changing certain amino acid residues in the framework regions of the heavy and light chain variable regions. The criteria used for humanization were as described previously, e.g., in U.S. Publication No. US 2009/0136500.

For cAb 0301, three humanized heavy chain variable regions and two humanized light chain variable regions were designed, for a total of six humanized antibodies, Ab1 to Ab6. For cAb 0302, two humanized heavy chain variable regions and three humanized light chain variable regions were designed, for a total of six humanized antibodies, Ab7 to Ab12. For cAb 0311, two humanized heavy chain variable regions and two humanized light chain variable regions were designed, for a total of four humanized antibodies, Ab13 to Ab16.

The sequences for each of the humanized heavy chain variable regions and humanized light chain variable regions, aligned with the sequences of the parental chimeric antibody variable regions and the sequences of the human acceptor variable framework regions are shown in FIGS. 1 (heavy chains) and 2 (light chains). The changes in humanized variable region sequences relative to the human acceptor variable framework region sequences are boxed. Each of the CDRs for each of the variable regions is shown in a boxed region, and labeled as "CDR" above the boxed sequences.

Table 8, below, shows the full sequences for the humanized heavy chains and humanized light chains of antibodies Ab 1

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to Ab 16. The name and SEQ ID NOs of the humanized heavy chain and humanized light chain of each of those antibodies is shown in Table 2.

TABLE 2

Humanized heavy chains and light chains of Ab1 to Ab16				
Humanized antibody	Humanized HC	SEQ ID NO	Humanized LC	SEQ ID NO
Ab1	h0301-H0	53	h0301-L0	60
Ab2	h0301-H1	54	h0301-L0	60
Ab3	h0301-H2	55	h0301-L0	60
Ab4	h0301-H0	53	h0301-L1	61
Ab5	h0301-H1	54	h0301-L1	61
Ab6	h0301-H2	55	h0301-L1	61
Ab7	h0302-H1	56	h0302-L0	62
Ab8	h0302-H1	56	h0302-L1	63
Ab9	h0302-H1	56	h0302-L2	64
Ab10	h0302-H2	57	h0302-L0	62
Ab11	h0302-H2	57	h0302-L1	63
Ab12	h0302-H2	57	h0302-L2	64
Ab13	h0311-H1	58	h0311-L0	65
Ab14	h0311-H1	58	h0311-L1	66
Ab15	h0311-H2	59	h0311-L0	65
Ab16	h0311-H2	59	h0311-L1	66

Example 5

Humanized Anti-CSF1R Antibodies Bind to Human and Cynomolgus CSF1R ECD, but not to Mouse CSF1R ECD

The 16 humanized antibodies were transiently expressed in CHO cells, as follows. CHO-3E7 cells were co-transfected with individual heavy and light chain expression plasmids at a mass ratio of 1 heavy chain plasmid to 2 light chain plasmids using polyethylenimine (PEI) at a DNA:PEI ratio of 1:5. Total DNA used per transfection was 1.5 μ g/ml of cells.

Humanized antibodies were purified from transfected cell supernatants using HiTrap Protein A HP columns (GE Healthcare) followed by further purification using Phenyl HP columns (GE Healthcare). Antibody containing supernatants were loaded onto HiTrap Protein A HP columns pre-equilibrated with PBS/0.5M NaCl. Antibody loaded columns were washed with 10 column volumes PBS/0.5M NaCl, and eluted with a mixed linear-step gradient of 0.1 M Glycine, pH 2.7/0.5 M NaCl directly into 100 μ l of 1M Tris buffer, pH 8.0. Antibody containing eluates were dialyzed against PBS, after which 2.4 M $(\text{NH}_4)_2\text{SO}_4$ (Sigma) was added to achieve a conductivity equal to that of 10 mM Potassium Phosphate pH7.0/1.2 M $(\text{NH}_4)_2\text{SO}_4$. Antibodies were then loaded on 1 ml Phenyl HP columns (GE Healthcare) pre-equilibrated with 10 mM Potassium Phosphate pH7.0/1.2 M $(\text{NH}_4)_2\text{SO}_4$. Antibody loaded columns were washed with 15 column volumes 10 mM Potassium Phosphate pH 7.0/1.2 M $(\text{NH}_4)_2\text{SO}_4$, and eluted with a 20 column volume gradient of 10 mM Potassium Phosphate, pH 7.0. Antibody containing fractions were pooled and dialyzed against PBS.

The humanized antibodies, along with their parental chimeric antibodies (cAbs), were assayed for binding to human, cynomolgus, and mouse CSF1R ECD, as follows.

Human CSF1R Binding Activity

Ninety-six well clear-bottom ELISA plates were coated overnight with 1 μ g/ml recombinant hCSF1R ECD.506-Fc (SEQ ID NO: 6; FivePrime Therapeutics) or Human M-CSF R Fc Chimera (R&D Systems) in PBS. The next morning, wells were washed four times with 0.05% Tween20 in PBS (PBST) and blocked with Blocker-Blotto (Pierce). Fifty μ l of

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0.5× serial dilutions of the humanized antibody or parental chimeric antibody, beginning with 2000 ng/ml, diluted 1:1 in Blocker-Blotto were added to the CSF1R-coated wells. After incubation at room temperature (RT) for 90 min, wells were washed four times with PBST, and a 1:5000 dilution of a peroxidase-conjugated Goat anti-Human kappa Light chain antibody (Sigma) in Blocker-Blotto was added to each well. After incubation at RT for 60 min, wells were washed four times with PBST, and 50 µl o-phenylenediamine dihydrochloride peroxidase substrate (Sigma) was added to each well. After incubation at RT for 30 min, A450 values of each well were read directly on a SpectraMaxPlus spectrophotometer with SoftMaxPro software (Molecular Devices).

The results of that experiment is shown in FIG. 3. All of the humanized antibodies bound to human CSF1R ECD within the range of concentrations tested.

Cynomolgus CSF1R Binding Curve

The binding curve for each humanized antibody binding to cynomolgus CSF1R ECD was determined as described above for human CSF1R, except the wells of the clear-bottom ELISA plates were coated overnight with 2 ng/ml recombinant cynoCSF1R ECD-Fc (FivePrime Therapeutics, SEQ ID NO: 8, but without the 19 amino acid leader sequence).

The results of that experiment are shown in FIG. 4. All of the humanized antibodies bound to cynomolgus CSF1R ECD within the range of concentrations tested.

Mouse CSF1R Binding Curve

The binding curve for each humanized antibody binding to mouse CSF1R ECD was determined as described above for human CSF1R, except the wells of the clear-bottom ELISA plates were coated overnight with 2 ng/ml recombinant mCSF1R ECD-Fc (FivePrime Therapeutics, SEQ ID NO: 93).

The results of that experiment are shown in FIG. 5. None of the humanized antibodies, or the parental chimeric antibodies, detectably bound to mouse CSF1R ECD over the range of concentrations tested.

Calculation of EC50s

Table 3 shows the EC50, calculated using the non-linear regression (curve-fit) analysis algorithm of the GraphPad Prism software (GraphPad Software) for each humanized antibody binding to human CSF1R ECD and cynomolgus CSF1R ECD. Because none of the chimeric antibodies detectably bound to mouse CSF1R ECD, an EC50 could not be calculated from that data. Table 3 also includes the calculated EC50s for the parental chimeric antibodies.

TABLE 3

Binding activity of humanized anti-CSF1R antibodies		
Humanized antibody	Human CSF1R ECD EC50 (ng/ml)	Cynomolgus CSF1R ECD EC50 (ng/ml)
cAb 0301	11.4	15.18
h0301-L0H0	13.4	15.11
h0301-L0H1	14.23	14.39
h0301-L0H2	14.77	13.79
h0301-L1H0	13.35	11.93
h0301-L1H1	16.47	16.66
h0301-L1H2	16.23	16.59
cAb 0302	15.94	17.34
h0302-L0H1	14.64	466.5
h0302-L1H1	21.43	1058
h0302-L2H1	7.741	66.04
h0302-L0H2	17.85	154.9
h0302-L1H2	22.1	172.5
h0302-L2H2	10.15	17.96
cAb 0311	17.65	20.06

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TABLE 3-continued

Binding activity of humanized anti-CSF1R antibodies		
Humanized antibody	Human CSF1R ECD EC50 (ng/ml)	Cynomolgus CSF1R ECD EC50 (ng/ml)
h0311-L0H1	13.12	21.65
h0311-L1H1	14.32	30.88
h0311-L0H2	11.54	17.47
h0311-L1H2	13.26	20.27

Example 6

Humanized Anti-CSF1R Antibodies Inhibit Ligand-Induced

CSF1R phosphorylation

CSF1R is phosphorylated in the presence of ligands CSF1 or IL34. The humanized antibodies, along with their parental chimeric antibodies (cAbs), were tested for their ability to inhibit CSF1R phosphorylation induced by either ligand, as follows.

Inhibition of CSF1-Induced Phosphorylation

CSF1R (SEQ ID NO: 2)-transfected CHO cells were incubated with serial dilutions of each humanized antibody or a parental chimeric antibody, beginning at 8 mg/ml, for 60 min on ice, after which 3.3 nM of human CSF1 (M-CSF, R&D Systems) was added to the cells. (For the 0301 series of humanized antibodies, serial dilutions beginning at 2 mg/ml of humanized antibody and parental chimeric antibody was used.) The cells were incubated for 3 minutes at 37° C., and then lysed by addition of 1/10× volume of 10× cell lysis buffer (Cell Signaling Technology). The amount of phosphorylated CSF1R in the cell lysates was quantified using a human phospho-M-CSF R ELISA kit (R&D Systems) according to the manufacturer's instructions.

The results of that experiment are shown in FIGS. 6A to 6C. All of the humanized antibodies were able to inhibit human CSF1-induced phosphorylation of human CSF1R ECD within the range of concentrations tested.

Inhibition of IL34-Induced Phosphorylation

CSF1R (SEQ ID NO: 2)-transfected CHO cells were incubated with 0.002 to 8 mg/ml of each humanized antibody or a parental chimeric antibody for 60 min on ice, after which 3.3 nM of human IL34 (FivePrime Therapeutics; SEQ ID NO: 68) was added to the cells. The cells were incubated for 3 minutes at 37° C., and then lysed by addition of 1/10× volume of 10× cell lysis buffer (Cell Signaling Technology). The amount of phosphorylated CSF1R in the cell lysates was quantified using a human phospho-M-CSF R ELISA kit (R&D Systems) according to the manufacturer's instructions.

The results of that experiment are shown in FIGS. 7A to 7C. All of the humanized antibodies were able to inhibit human IL34-induced phosphorylation of human CSF1R within the range of concentrations tested.

Example 7

Humanized Anti-CSF1R Antibodies Block Human CSF1 and Human IL34 Binding to Human and Cynomolgus CSF1R

Human CSF1/CSF1R Blocking Activity

The humanized antibodies, along with the parental chimeric antibodies (cAbs), were tested for their ability to block human CSF1 binding to human and cynomolgus CSF1R ECD, as follows.

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Recombinant Human CSF1 (M-CSF; R&D Systems) was biotinylated using an NH₂-Biotin Labeling Kit (Dojindo Molecular Technologies). One hundred μ l of 1 μ g/ml biotinylated CSF1 in PBST/0.1% BSA was added to the wells of Reacti-Bind Streptavidin coated plates (Pierce) pre-blocked with SuperBlock blocking buffer (Pierce) according to the manufacturer's instructions. Fifty μ l of 0.5 \times serial dilutions of the humanized antibody or parental chimeric antibody, beginning with 2000 ng/ml, was incubated with 50 ng/ml hCSF1R ECD.506-Fc (SEQ ID NO: 6; FivePrime Therapeutics) or 50 ng/ml cynoCSF1R ECD-Fc (FivePrime Therapeutics, SEQ ID NO: 8, but without the 19 amino acid leader sequence) in 100 μ l PBST/0.1% BSA for 90 min at RT, after which the admix was transferred to one or more wells of a ligand-coated plate. After 90 min at RT, wells were washed with PBST, and a 1:5000 dilution of an Fc-fragment-specific peroxidase-conjugated goat anti-human IgG (Jackson Immuno Research) in PBST/0.1% BSA was added to each well. After incubation at RT for 60 min, wells were washed with PBST/0.1% BSA, and o-phenylenediamine dihydrochloride peroxidase substrate (Sigma) was added to each well. After incubation at RT for 30 min, A450 values of each well were read directly on a SpectraMaxPlus spectrophotometer with SoftMaxPro software (Molecular Devices).

The results of that experiment for cynomolgus CSF1R are shown in FIGS. 8A to 8C. All of the humanized antibodies based on Fabs 0301 and 0311 were able to block human CSF1 binding to cynomolgus CSF1R ECD within the range of concentrations tested. None of the humanized antibodies based on Fab 0302 showed similar blocking activity in that experiment compared to the blocking activity of cAb 0302. Human IL34/CSF1R Blocking Activity

The humanized antibodies were tested for their ability to block human IL34 binding to human CSF1R ECD. The blocking activity of each humanized antibody was determined as described above for blocking of CSF1, except recombinant human IL34 (FivePrime Therapeutics; SEQ ID NO: 68) was biotinylated using an NH₂-Biotin Labeling Kit (Dojindo Molecular Technologies), and then 100 μ l of 1 mg/ml biotinylated recombinant IL34 in PBST/0.1% BSA was added to the wells of Reacti-Bind Streptavidin coated plates (Pierce) pre-blocked with SuperBlock blocking buffer (Pierce) according to the manufacturer's instructions.

The results of that experiment for cynomolgus CSF1R are shown in FIGS. 9A to 9C. All of the humanized antibodies based on Fabs 0301 and 0311 were able to block human IL34 binding to cynomolgus CSF1R ECD within the range of concentrations tested. None of the humanized antibodies based on Fab 0302 showed similar blocking activity in that experiment compared to the blocking activity of cAb 0302. Calculation of IC₅₀s

Table 4 shows the IC₅₀, calculated using the non-linear regression (curve-fit) analysis algorithm of the GraphPad Prism software (GraphPad Software), for inhibition of ligand-induced CSF1R phosphorylation by each humanized antibody. Table 4 also shows the IC₅₀, calculated using the non-linear regression (curve-fit) analysis algorithm of the GraphPad Prism software (GraphPad Software), for blocking of ligand binding to CSF1R ECD by each humanized antibody. Finally, Table 4 shows the number of amino acids in the framework regions of the light and heavy chain of each humanized antibody that were back-mutated to the corresponding mouse amino acid residue. For example, humanized antibody h0301L1H1 has one amino acid in a light chain framework region that was back-mutated to the mouse amino acid, and one amino acid in the heavy chain framework regions that was back-mutated to the mouse amino acid.

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Referring to FIGS. 1 and 2, the back-mutated amino acid in the light chain framework is at position 1 in framework 1, and the back-mutated amino acid in the heavy chain is at position 71 in framework 3 according to Kabat numbering (see FIG. 1B).

TABLE 4

Blocking activity of humanized anti-CSF1R antibodies					
Humanized Antibody	Human CSF1/ Human CSF1R ECD IC50 (ng/ml)	Human IL34/ Human CSF1R ECD IC50 (ng/ml)	Human CSF1/ CynoCSF1R ECD IC50 (ng/ml)	Human IL34/ CynoCSF1R ECD IC50 (ng/ml)	Back-mutated mouse residues in FRs (L + H)
cAb0301	307.2	312.2	22.01	29.53	
h0301-L0H0	1031	433	27.64	35.92	0 + 0
h0301-L0H1	778.1	452.6	27.45	36.43	0 + 1
h0301-L0H2	1317	480.9	28.05	37.37	0 + 4
h0301-L1H0	6150	378	25.53	34.84	1 + 0
h0301-L1H1	814.2	384.4	31.07	42.41	1 + 1
h0301-L1H2	682.1	397.1	27.77	36.53	1 + 4
cAb0302	263.5	350.8	33.09	49.38	
h0302-L0H1	927.7	615	15.55	2.00E+12	0 + 2
h0302-L1H1	742	363.7	60.49	676.4	1 + 2
h0302-L2H1	384	303.1	89827	509.1	3 + 2
h0302-L0H2	438.2	474.2	none	248.1	0 + 5
h0302-L1H2	597.8	495.3	1085	541.3	1 + 5
h0302-L2H2	354.4	240.1	837.6	278.7	3 + 5
cAb 0311	577	994.2	43.47	52.1	
h0311-L0H1	291.3	343.2	32.47	50.4	0 + 2
h0311-L1H1	507.5	667.4	24.68	53.69	2 + 2
h0311-L0H2	435.5	633.3	25.96	40.79	0 + 5
h0311-L1H2	419	578.2	30.76	48.56	2 + 5

Example 8

Humanized Anti-CSF1R Antibody Binding Constants

The k_{on} , k_{off} , and K_D for binding to human CSF1R ECD was determined for each of the humanized antibodies as follows.

Binding kinetics of anti-CSF1R humanized antibodies to CSF1R ECD was determined using Biacore T100 Surface Plasmon Resonance (SPR) (GE Healthcare Life Sciences, Piscataway, N.Y.). Each of the humanized anti-CSF1R antibodies was captured on a CM5 sensor chip immobilized with anti-Human IgG antibody using the Human antibody capture kit (GE Healthcare Life Sciences, Piscataway, N.Y.) at 150RU so that the Rmax value for hCSF1R ECD.506 (SEQ ID NO: 5) binding was 100RU. Rmax values of less than 150RU are recommended for accurately determining kinetic values. 10 mM Hepes buffered saline, pH 7.4, with 0.05% Tween20 (HPS-P; GE Healthcare Life Sciences, Piscataway, N.Y.) was used as the running and dilution buffer. hCSF1R ECD.506 was injected at six concentrations (90 nM, 30 nM, 10 nM, 3.33 nM, 1.11 nM, and 0 nM) for 2 minutes and dissociation was observed for 5 minutes to determine humanized antibody/hCSF1R ECD binding kinetic parameters. The association constant, dissociation constant, affinity, and binding capacity of each of the Fabs for human CSF1R ECD was calculated using the Biacore T100 Evaluation software package using the 1:1 binding model.

The results of the kinetic determinations are shown in Table 5.

TABLE 5

Humanised antibody binding affinity for human CSF1R			
huAbAb	k_a ($M^{-1}s^{-1}$)	K_d (s^{-1})	K_D (nM)
huAb 0301-L0H0	3.22×10^6	1.11×10^{-03}	0.35
huAb 0301-L0H1	3.56×10^6	1.22×10^{-03}	0.34
huAb 0301-L0H2	2.32×10^6	6.60×10^{-04}	0.28
huAb 0301-L1H0	3.29×10^6	1.15×10^{-03}	0.35
huAb 0301-L1H1	2.87×10^6	9.21×10^{-04}	0.32
huAb 0301-L1H2	2.95×10^6	7.42×10^{-04}	0.25
huAb 0302-L0H1	3.54×10^6	3.69×10^{-03}	1.04
huAb 0302-L1H1	3.47×10^6	4.04×10^{-03}	1.17
huAb 0302-L2H1	1.60×10^6	9.14×10^{-04}	0.57
huAb 0302-L0H2	3.40×10^6	1.79×10^{-03}	0.53
huAb 0302-L1H2	2.71×10^6	1.53×10^{-03}	0.56
huAb 0302-L2H2	1.84×10^6	8.40×10^{-04}	0.46
huAb 0311-L0H1	1.22×10^6	5.40×10^{-04}	0.44
huAb 0311-L1H1	1.32×10^6	6.64×10^{-04}	0.50
huAb 0311-L0H2	1.34×10^6	4.73×10^{-04}	0.35
huAb 0311-L1H2	1.51×10^6	6.09×10^{-04}	0.40

All but two of the humanized antibodies showed sub-nanomolar binding affinities for human CSF1R ECD, and the remaining two humanized antibodies showed binding affinities for human CSF1R ECD of less than 2 nM.

Example 9

Humanized Anti-CSF1R Antibodies Block Ligand-Induced Phosphorylation

Based on the data above, including CSF1R binding and ligand inhibition, and the likelihood of immunogenicity for each humanized antibody, three humanized antibodies were selected for further study: 0301-L0H0, 0301-L1H0, and 0311-L0H1.

After confirming that 0301-L0H0, 0301-L1H0, and 0311-L0H1 each bind to CSF1R on the surface of cells (data not shown), each of the antibodies was tested for the ability to block ligand-induced CSF1R phosphorylation in CHO cells, as described in Example 6.

The results of that experiment are shown in FIG. 10. All three of the humanized antibodies tested blocked both CSF1-induced (A) and IL34-induced (B) phosphorylation of CSF1R in CHO cells. Table 6 shows the IC50 for blocking of ligand-induced CSF1R phosphorylation for each antibody.

TABLE 6

Ligand-induced phosphorylation blocking IC50 for humanized antibodies		
Humanized antibody	CSF1 blocking IC50 (ng/ml)	IL34 blocking IC50 (ng/ml)
0301-L0H0	305.4	340.8
0301-L1H0	213.2	242.2
0311-L0H1	127.2	337.6

Example 10

Humanized Anti-CSF1R Antibodies Block Ligand-Induced Proliferation/Survival Responses of Primary Human Monocytes

Humanized antibodies 0301-L0H0, 0301-L1H0, and 0311-L0H1 were tested for their ability to block ligand-induced monocyte proliferation/survival responses as follows.

Human peripheral blood mononuclear cells (PBMCs) were isolated from healthy donor blood by centrifugation onto a Ficoll-Paque cushion (GE Healthcare Bio-Sciences) according to the manufacturer's instructions. Peripheral blood monocytes were subsequently isolated from the recovered PBMC fraction by centrifugation onto a 48.5% Percoll™ cushion (GE Healthcare Bio-Sciences). After recovery from the Percoll™ cushion, the purified peripheral blood monocytes were stimulated with 162 μ M recombinant human CSF1 or 1.6 nM recombinant human IL34 (both from R&D Systems) in the presence or absence of serial dilutions of humanised antibody 0301-L0H0, humanised antibody 0301-L1H0, or humanised antibody 0311-L0H1. After incubation at 37° C. for 48 hours, relative cellular ATP content of each individual culture was assessed using CellTiter-Glo® reagent (Promega) according to the manufacturer's instructions. In this assay, relative cellular ATP content is directly proportional to the number of viable cells in culture, and thus reflects monocyte proliferation/survival responses.

The results of that experiment are shown in FIG. 11. All three of the humanized antibodies tested were able to block monocyte proliferation/survival responses following CSF1 (A) or IL34 (B) stimulation. Table 7 shows the IC50s for blocking of ligand-induced monocyte proliferation/survival responses for each antibody. The values shown in Table 7 represent the range observed from the three different primary donors tested.

TABLE 7

Monocyte proliferation/survival blocking IC50 for humanized antibodies		
Humanized antibody	CSF1 blocking IC50 (ng/ml)	IL34 blocking IC50 (ng/ml)
0301-L0H0	31.9-77.5	12.2-29.9
0301-L1H0	19.0-71.9	10.5-30.6
0311-L0H1	75.9-134.8	26.9-152.2

Example 11

Humanized Anti-CSF1R Antibodies do not Directly Stimulate Primary Human Monocyte Proliferation or Survival Responses

Humanized antibodies 0301-L0H0, 0301-L1H0, and 0311-L0H1 were tested for their ability to directly stimulate primary monocyte proliferation and/or survival, as follows.

Human peripheral blood monocytes were isolated as described in Example 10. Serial dilutions of humanised antibody 0301-L0H0, humanised antibody 0301-L1H0, or humanised antibody 0311-L0H1 were added to the monocytes in the absence of stimulation either by exogenous CSF1 or by exogenous IL34. After incubation at 37° C. for 48 hours, relative ATP content of each individual culture was assessed using CellTiter Glo0 reagent (Promega) as in Example 10. The experiment was carried out on peripheral blood monocytes from three different donors.

The results of that experiment are shown in FIG. 12. None of the humanized antibodies stimulated primary monocyte proliferation or survival in either of the primary monocyte preparations tested.

TABLE OF SEQUENCES

Table 8 provides certain sequences discussed herein. All polypeptide and antibody sequences are shown without leader sequences, unless otherwise indicated.

TABLE 8

Sequences and Descriptions					
SEQ ID NO	Description	Sequence			
1	hCSF1R (full-length) no leader sequence)	IPVIEPSVPE	LVVKPGATVT	LRCVGNNGSVE	WDGPPSPHWT
		STNNATFQNT	GTyrCTEPGD	PLGGSAAIHL	YVKDPAWPWN
		DQDALLPCLL	TDPVLEAGVS	LVRVRGRPLM	RHTNYSFSPW
		IQSQDYQCSA	LMGGRKVMIS	SIRLKVQKVI	PGPPALTLPV
		AQIVCSASSV	DVNFDFVLQH	NNTKLAIPQQ	SDFHNNRYQK
		FQHAGNYSVCV	ASNVQGHST	SMFFRVVESA	YLNLSSEQNL
		NLKMVEAYP	GLQGFNWTYL	GPFSHQPEP	KLANATTKDT
		RLKPSEAGRY	SFLARNPGGW	RALTFELTLR	YPPEVSVIWT
		AASGYPPQNV	TWLQCSGHTD	RCDEAQVLQV	WDDPYPEVLS
		SLLTVETLEH	NQTYECRAHN	SVGSGSWAFI	PISAGATHP
		VACMSIMALL	LLLLLLLLLYK	YKQKPKYQVR	WKIIESYEGN
		PYNEKWEFPR	NNLQFGKTLG	AGAFGKVVEA	TAFGLGKEDA
		STAHADKEKA	LMSELKIMSH	LQGHENIVNL	LGACTHGGPV
		DLNLFRLRKA	EAMLGPSLSP	GQDPEGGVDT	KNIHLEKKYV
		VDTYVEMRPV	STSSNDSFSE	QDLKEDGRP	LELRDLLHFS
		ASKNCIHRDV	AARNVLLTNG	HVAKIGDFGL	ARDIMNDSNY
		KWMAPEIFD	CVYTVQSDVW	SYGILLWEIF	SLGLNPYPGI
		KDGYQMAQPA	FAPKNIYSIM	QACWALEPTH	RPTFQQICSF
		ERDYNLPS	SRSGGSGSSS	SELEEESSSE	HLTCCEQGD
		QFC			
2	hCSF1R (full length, + leader sequence)	MGPVGLLLLL	VATAWHGQGI	PVIEPSVPEL	VVKPGATVTL
		DGPPSPHWT	YSDGSSSILS	TNNATFQNTG	TYRCTEPGDP
		VKDPARPWNV	LAQEVVVFED	QDALLPCLLT	DPVLEAGVSL
		HTNYSFSPWH	GFTIHRAKFI	QSQDYQCSAL	MGGRKVMIS
		GPPALTLPVA	ELVRIRGEAA	QIVCSASSVD	VNFDFVLQHN
		DFHNNRYQKV	LTLNLDQVDF	QHAGNYSVA	SNVQGHST
		LNLSSQNLI	QEVTVGEGLN	LKMVEAYPG	LQGFNWTYL
		LANATTKDTY	RHTFTLSLPR	LKPSEAGRY	FLARNPGGWR
		PPEVSVIWT	INGSGTLLCA	ASGYPPQNV	WLQCSGHTDR
		DDPYPEVLSQ	EPFHKVTVQS	LLTVETLEHN	QTYECRAHNS
		ISAGATHHP	DEFLFTPVV	ACMSIMALLL	LLLLLLLLLYK
		KIIESYEGNS	YTFIDPTQLP	YNEKWEFPRN	NLQFGKTLGA
		AFGLGKEDAV	LKVAVKMLKS	TAHADEKEAL	MSELKIMSHL
		GACTHGGPVL	VITEYCCYGD	LLNLFRLRKA	AMLGPSLSPG
		NIHLEKKYVR	RDSGFSSQGV	DTYVEMRPVS	TSSNDSFSEQ
		ELRDLHFS	QVAQGMFLA	SKNCIHRDVA	ARNVLLTNGH
		RDIMNDSNYI	VKGARLPVK	WMAPEIFDC	VYTVQSDVMS
		LGLNPYPGIL	VNSKFYKLVK	DGYQMAQPAF	APKNIYSIMQ
		PTFQQICSF	QEQAQEDRRE	RDYTNLPS	RSGSGSSS
		LTCCEQGDIA	QPLLQPNNYQ	FC	
5	hCSF1R ECD.506	IPVIEPSVPE	LVVKPGATVT	LRCVGNNGSVE	WDGPPSPHWT
		STNNATFQNT	GTyrCTEPGD	PLGGSAAIHL	YVKDPAWPWN
		DQDALLPCLL	TDPVLEAGVS	LVRVRGRPLM	RHTNYSFSPW
		IQSQDYQCSA	LMGGRKVMIS	SIRLKVQKVI	PGPPALTLPV
		AQIVCSASSV	DVNFDFVLQH	NNTKLAIPQQ	SDFHNNRYQK
		FQHAGNYSVCV	ASNVQGHST	SMFFRVVESA	YLNLSSEQNL
		NLKMVEAYP	GLQGFNWTYL	GPFSHQPEP	KLANATTKDT
		RLKPSEAGRY	SFLARNPGGW	RALTFELTLR	YPPEVSVIWT
		AASGYPPQNV	TWLQCSGHTD	RCDEAQVLQV	WDDPYPEVLS
		SLLTVETLEH	NQTYECRAHN	SVGSGSWAFI	PISAGATHP
6	hCF1SR ECD.506-Fc	IPVIEPSVPE	LVVKPGATVT	LRCVGNNGSVE	WDGPPSPHWT
		STNNATFQNT	GTyrCTEPGD	PLGGSAAIHL	YVKDPAWPWN
		DQDALLPCLL	TDPVLEAGVS	LVRVRGRPLM	RHTNYSFSPW
		IQSQDYQCSA	LMGGRKVMIS	SIRLKVQKVI	PGPPALTLPV
		AQIVCSASSV	DVNFDFVLQH	NNTKLAIPQQ	SDFHNNRYQK
		FQHAGNYSVCV	ASNVQGHST	SMFFRVVESA	YLNLSSEQNL
		NLKMVEAYP	GLQGFNWTYL	GPFSHQPEP	KLANATTKDT
		RLKPSEAGRY	SFLARNPGGW	RALTFELTLR	YPPEVSVIWT
		AASGYPPQNV	TWLQCSGHTD	RCDEAQVLQV	WDDPYPEVLS
		SLLTVETLEH	NQTYECRAHN	SVGSGSWAFI	PISAGATHP
		CPAPELLGGP	SVFLFPPKPK	DTLMISRTPE	VTCVVVDVSH
		VDGVEVHNAK	TKPREEQYNS	TYRVVSVLTV	LHQDWLNGKE
		PAPIEKTISK	AKGQPREPQV	YTLPPSRDEL	TKNQVSLTCL
		VEWESNGQPE	NNYKTTTPVL	DSGGSFFLYS	KLTVDKSRWQ
		HEALHNHYTQ	KSLSLSPGK		

TABLE 8-continued

Sequences and Descriptions					
SEQ ID NO	Description	Sequence			
7	cynoCSF1R ECD (with leader sequence)	MGPGLVLLLL	VVTAWHGQGI	PVIEPSGPPEL	VVKPGETVTL RCVGNCSVEW DGPISPHWTL YSDGPSSVLT TTNATFQNTR TYRCTEPGDP LGGSAAIHLY VKDPPARPWNV LAKEVVVFED QDALLPCLLT DPVLEAGVSL VRLRGRPLLR HTNYSFSPWH GFTIHRAKFI QGQDYQCSAL MGSRKVMSIS IRLKVQKVIP GPPALTLVPA ELVRIRGEAA QIVCSASNID VDFDVFLQHN TTKLAIPQRS DFHDNRYQKV LTLSLGQVDF QHAGNYSQVA SNVQGHKSTS MFFRVVESAY LDLSSEQNLI QEVTVGEGLN LKVMVEAYPG LQGFNWTYLG PFSHQPEPK LANATTKDTY RHTFTLSLPR LKPSEAGRYS FLARNPGGWR ALTFELTLRY PPEVSVIWT S INSGTLLCA ASGYQPQNV T WLQCAGHTDR CDEAQLQVW VDPHPPEVLSQ EPPQKVTVQS LLTAETLEHN QTYECRAHNS VSGSGWAFIP ISAGAR
8	cynoCSF1R ECD-Fc (with leader sequence)	MGPGLVLLLL	VVTAWHGQGI	PVIEPSGPPEL	VVKPGETVTL RCVGNCSVEW DGPISPHWTL YSDGPSSVLT TTNATFQNTR TYRCTEPGDP LGGSAAIHLY VKDPPARPWNV LAKEVVVFED QDALLPCLLT DPVLEAGVSL VRLRGRPLLR HTNYSFSPWH GFTIHRAKFI QGQDYQCSAL MGSRKVMSIS IRLKVQKVIP GPPALTLVPA ELVRIRGEAA QIVCSASNID VDFDVFLQHN TTKLAIPQRS DFHDNRYQKV LTLSLGQVDF QHAGNYSQVA SNVQGHKSTS MFFRVVESAY LDLSSEQNLI QEVTVGEGLN LKVMVEAYPG LQGFNWTYLG PFSHQPEPK LANATTKDTY RHTFTLSLPR LKPSEAGRYS FLARNPGGWR ALTFELTLRY PPEVSVIWT S INSGTLLCA ASGYQPQNV T WLQCAGHTDR CDEAQLQVW VDPHPPEVLSQ EPPQKVTVQS LLTAETLEHN QTYECRAHNS VSGSGWAFIP ISAGARGSEP KSSDKTHTCP PCPAPELLGG PSVFLFPPKP KDTLMISRT EVTCTVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ VYTLPPSRDE LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTPPV LDSDGSFFLY SKLTVDKSRW QQGNVFSQSV MHEALHNYT QKSLSLSPGK
3	Light chain leader sequence	METDTLLLV	LLLWVPGSTG		
4	Heavy chain leader sequence	MAVLGLLLCL	VTFPSCVLS		
9	Fab 0301 heavy chain variable region	EVQLQQSGPE	LVRPGASVKM	SCKASGYTFT	DNYMIWVKQS HGKSLEWIGD INPYNGGTTF NQKFKGKATL TVEKSSSTAY MQLNSLTSED SAVVYCARES PYFSNLYVMD YWGQGTSTTV S
10	Fab 0301 light chain variable region	NIVLTQSPAS	LAVSLGQRAT	ISCKASQSVD	YDGDNYMNWY QQKPGQPPKL LIYAASNLES GIPARFSGSG SGTDFTLNIH PVEEEDAATY YCHLSNEDLS TFGGGTKLEI K
11	Fab 0302 heavy chain variable region	EIQLQQSGPE	LVKPGASVKM	SCKASGYTFS	DFNIHWVKQK PGQGLEWIGY INPYTDVTYV NEKFKGKATL TSDRSSSTAY MDLSSLTSED SAVVYCASYF DGTFDYALDY WGQGTSTITVS S
12	Fab 0302 light chain variable region	DVVVTQTPAS	LAVSLGQRAT	ISCRASESVD	NYGLSFMNWF QQKPGQPPKL LIYTASNLES GIPARFSGGG SRTDFTLTID PVEADDAATY FCQQSKELPW TFGGGTRLEI K
13	Fab 0311 heavy chain variable region	EIQLQQSGPD	LMKPGASVKM	SCKASGYIFT	DYNMHWVKQN QGKSLEWMGE INPNNGVVVY NQKFKGTTLT TVDKSSSTAY MDLHSLTSED SAVVYCTRAL YHSNFGWYFD SWGKGTTLTV S
14	Fab 0311 light chain variable region	DIVLTQSPAS	LAVSLGQRAT	ISCKASQSVD	YDGDSHMNWY QQKPGQPPKL LIYTASNLES GIPARFSGSG SGADFTLTIH PVEEEDAATY YCQQGNEDPW TFGGGTRLEI K
15	0301 heavy chain CDR1	GYTFTDNYMI			
16	0301 heavy chain CDR2	DINPYNGGTT	FNQKFKG		

TABLE 8-continued

Sequences and Descriptions	
SEQ ID NO Description	Sequence
17 0301 heavy chain CDR3	ESPYFSNLYV MDY
18 0301 light chain CDR1	KASQSVDDYDG DNYMN
19 0301 light chain CDR2	AASNLES
20 0301 light chain CDR3	HLSNEDLST
21 0302 heavy chain CDR1	GYTFSDFNIH
22 0302 heavy chain CDR2	YINPYTDVTV YNEKFKG
23 0302 heavy chain CDR3	YFDGTFDYAL DY
24 0302 light chain CDR1	RASESVDNYG LSFMN
25 0302 light chain CDR2	TASNLES
26 0302 light chain CDR3	QQSKELPWT
27 0311 heavy chain CDR1	GYIFTDYNMH
28 0311 heavy chain CDR2	EINPNNGVVV YNQKFKG
29 0311 heavy chain CDR3	ALYHSNFGWY FDS
30 0311 light chain CDR1	KASQSVDDYDG DSHMN
31 0311 light chain CDR2	TASNLES
32 0311 light chain CDR3	QQGNEDPWT
33 cAb 0301 heavy chain	EVQLQQSGPE LVRPGASVKM SCKASGYTFT DNYMIWVKQS HGKSLEWIGD INPYNGGTTF NQKFKGKATL TVEKSSSTAY MQLNSLTSED SAVYYCARES PYFSNLYVMD YWQGQTSVTV SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ SSGLYSLSSV VTPSSSLGT KTYTCNVNDHK PSNTKVDKRV ESKYGPPCPP CPAPEFLGGP SVFLFPPKPK DTLMISRTPE VTCVVVDVSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS TYRVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTPPVLD DSGGSFFLYS RLTVDKSRWQ EGNVFSCSVM HEALHNHYTQ KSLSLSLGK
34 cAb 0301 light chain	NIVLTQSPAS LAVSLGQRAT ISCKASQSV YDGDNYMNWY QQKPGQPPKL LIYAASNLES GIPARFSGSG SGTDFTLNIH PVEEEDAATY YCHLSNEDLS TFGGGTKLEI KRTVAAPSVF IFPPSDEQLK SGTVSVVCLL NNFYPREAKV QWKVDNALQS GNSQESVTEQ DSKDSTYSLS STLTLKADY EKHKVYACEV THQGLSSPVT KSFNRGEC
35 cAb 0302 heavy chain	EIQLQQSGPE LVKPGASVKM SCKASGYTFS DFNHFWVKQK PGQGLEWIGY INPYTDVTVY NEKFKGKATL TSDRSSSTAY MDLSSLTSED SAVYYCASYF DGTDFDYALDY WQGQTSITVS SASTKGPSVF PLAPCSRSTS ESTAALGCLV KDYFPEPVTV SWNSGALTS VHTFPAVLQS SGLYSLSSVV TVPSSSLGTK TYTCNVNDHKP SNKVDKRV ESKYGPPCPP CPAPEFLGGP VFLFPPKPKD TLMISRTPEV TCVVVDVSQ EDPEVQFNWY VDGVEVHNAK KPREEQFNS YRVSVLTVL HQDWLNGKEY KCKVSNKGLP SSIEKTISKA KGQPREPQVY TLPPSQEEMT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTPPVLD SDGSFFLYSR LTVDKSRWQ EGNVFSCSVMH EALHNHYTQK SLSLSLGK

TABLE 8-continued

Sequences and Descriptions					
SEQ ID NO	Description	Sequence			
36 cAb 0302	light chain	DVVVTQTPAS	LAVSLGQRAT	ISCRASESVD	NYGLSFMNWF
		LIYTASNLES	GIPARFSGGG	SRTDFTLTID	PVEADDAATY
		TFGGGTRLEI	KRTVAAPSVF	IFPPSDEQLK	SGTASVVCLL
		QWKVDNALQS	GNSQESVTEQ	DSKDSTYSL	STLTLSKADY
		THQGLSSPVT	KSPNRGEC		EKHKVYACEV
37 cAb 0311	heavy chain	EIQLQQSGPD	LMKPGASVKM	SCKASGYIFT	DYNMHVVKQN
		INPNNGVVVY	NQKFKGTTTL	TVDKSSSTAY	MDLHSLTSED
		YHSNFGWYFD	SWGKGTTTLV	SSASTKGPSV	FPLAPCSRST
		VKDYFPEPVT	VSWNSGALTS	GVHTFPAVLQ	SSGLYSLSSV
		KTYTCNVDPK	PSNTKVDKRV	ESKYGPPCPP	CPAPEFLGGP
		DTLMISRTP	VTCVVVDVSQ	EDPEVQFNWY	VDGVEVHNAK
		TYRVVSVLTV	LHQDWLNGKE	YKCKVSNKGL	PSSIEKTISK
		YTLPPSQEEM	TKNQVSLTCL	VKGFYPSDIA	VEWESNGQPE
		DSGGSFFLYS	RLTVDKSRWQ	EGNVFSCSVM	HEALHNHYTQ
					KSLSLSLGK
38 cAb 0311	light chain	DIVLTQSPAS	LAVSLGQRAT	ISCKASQSVD	YDGDSHMNWY
		LIYTASNLES	GIPARFSGSG	SGADFTLTIH	PVEEEDAATY
		TFGGGTRLEI	KRTVAAPSVF	IFPPSDEQLK	SGTASVVCLL
		QWKVDNALQS	GNSQESVTEQ	DSKDSTYSL	STLTLSKADY
		THQGLSSPVT	KSPNRGEC		EKHKVYACEV
39 h0301-H0	heavy chain variable region	QVQLVQSGAE	VKKPGSSVKV	SCKASGYTFT	DNYMIWVRQA
		INPYNGGTF	NQKFKGRVTI	TADKSTSTAY	MELSSLRSED
		PYFSNLYVMD	YWGQGLTVTV	SS	TAVYYCARES
40 h0301-H1	heavy chain variable region	QVQLVQSGAE	VKKPGSSVKV	SCKASGYTFT	DNYMIWVRQA
		INPYNGGTF	NQKFKGRVTI	TVDKSTSTAY	MELSSLRSED
		PYFSNLYVMD	YWGQGLTVTV	SS	TAVYYCARES
41 h0301-H2	heavy chain variable region	QVQLVQSGAE	VKKPGSSVKV	SCKASGYTFT	DNYMIWVRQA
		INPYNGGTF	NQKFKGRATL	TVDKSTSTAY	MELSSLRSED
		PYFSNLYVMD	YWGQGLTVTV	SS	TAVYYCARES
42 H0302-H1	heavy chain variable region	QVQLVQSGAE	VKKPGSSVKV	SCKASGYTFS	DFNIHWVRQA
		INPYTDVTY	NEKFKGRVTI	TSBKSTSTAY	MELSSLRSED
		DGTFDYALDY	WGQGLTVTVS	S	TAVYYCASYF
43 H0302-H2	heavy chain variable region	QVQLVQSGAE	VKKPGSSVKV	SCKASGYTFS	DFNIHWVRQA
		INPYTDVTY	NEKFKGRATL	TSBKSTSTAY	MELSSLRSED
		DGTFDYALDY	WGQGLTVTVS	S	TAVYYCASYF
44 H0311-H1	heavy chain variable region	QVQLVQSGAE	VKKPGSSVKV	SCKASGYIFT	DYNMHVVRQA
		INPNNGVVVY	NQKFKGRVTI	TVDKSTSTAY	MELSSLRSED
		YHSNFGWYFD	SWGQGLTVTV	SS	TAVYYCTRAL
45 H0311-H2	heavy chain variable region	QVQLVQSGAE	VKKPGSSVKV	SCKASGYIFT	DYNMHVVRQA
		INPNNGVVVY	NQKFKGTTTL	TVDKSTSTAY	MELSSLRSED
		YHSNFGWYFD	SWGQGLTVTV	SS	TAVYYCTRAL
46 h0301-L0	light chain variable region	EIVLTQSPAT	LSLSPGERAT	LSCKASQSVD	YDGDNYMNWY
		LIYAASNLES	GIPARFSGSG	SGDFTLTIS	SLEPEDFAVY
		TFGGGTKVEI	K		YCHLSNEDLS
47 h0301-L1	light chain variable region	NIVLTQSPAT	LSLSPGERAT	LSCKASQSVD	YDGDNYMNWY
		LIYAASNLES	GIPARFSGSG	SGDFTLTIS	SLEPEDFAVY
		TFGGGTKVEI	K		YCHLSNEDLS
48 H0302-L0	light chain variable region	EIVLTQSPAT	LSLSPGERAT	LSCRASESVD	NYGLSFMNWF
		LIYTASNLES	GIPARFSGSG	SGDFTLTIS	SLEPEDFAVY
		TFGGGTKVEI	K		YCHLSNEDLS

TABLE 8-continued

Sequences and Descriptions					
SEQ ID NO Description	Sequence				
49 H0302-L1 light chain variable region	EIVLTQSPAT LIYTASNLES TFGQGTKVEI	LSLSPGERAT GIPARFSGSG K	LSCRASESVD SRTDFTLTIS	NYGLSFMNMY SLEPEDFAVY	QQKPGQAPRL YCQQSKELPW
50 H0302-L2 light chain variable region	EIVVTQSPAT LIYTASNLES TFGQGTKVEI	LSLSPGERAT GIPARFSGSG K	LSCRASESVD SRTDFTLTIS	NYGLSFMNWF SLEPEDFAVY	QQKPGQAPRL YCQQSKELPW
51 H0311-L0 light chain variable region	EIVLTQSPAT LIYTASNLES TFGQGTKVEI	LSLSPGERAT GIPARFSGSG K	LSCKASQSVD SGTDFTLTIS	YDGDSHMNWY SLEPEDFAVY	QQKPGQAPRL YCQQGNEDPW
52 H0311-L1 light chain variable region	DIVLTQSPAT LIYTASNLES TFGQGTKVEI	LSLSPGERAT GIPARFSGSG K	LSCKASQSVD SGADFTLTIS	YDGDSHMNWY SLEPEDFAVY	QQKPGQAPRL YCQQGNEDPW
53 h0301-H0 heavy chain	QVQLVQSGAE INPYNGGTTF PYFSNLYVMD VKDYFPEPVT KTYTCNVNDHK DTLMISRTP TYRVVSVLTV YTLPPSQEEM DSDGSFFLYS	VKKPGSSVKV NQKFKGRVTI YWGQGTLLTV VSWNSGALTS PSNTKVDKRV VTCVVVDVSQ LHQDWLNGKE TKNQVSLTCL RLTVDKSRWQ	SCKASGYTFT TADKSTSTAY SSASTKGPSV GVHTFPAVLQ ESKYGPPCPP EDPEVQFNWY YKCKVSNKGL VKGFYPSDIA EGNVFSCSVM	DNYMIWVRQA MELSSLRSED FPLAPCSRST SSGLYSLSV CPAPEFLGGP VDGVEVHNAK PSSIEKTISK VEWESNGQPE HEALHNHYTQ	PGQGLEWMGD TAVYYCARES SESTAALGCL VTVPSSSLGT SVFLFPPKPK TKPREEQFNS AKGQPREPQV NNYKTPPVVL KSLSLSLGK
54 h0301-H1 heavy chain	QVQLVQSGAE INPYNGGTTF PYFSNLYVMD VKDYFPEPVT KTYTCNVNDHK DTLMISRTP TYRVVSVLTV YTLPPSQEEM DSDGSFFLYS	VKKPGSSVKV NQKFKGRVTI YWGQGTLLTV VSWNSGALTS PSNTKVDKRV VTCVVVDVSQ LHQDWLNGKE TKNQVSLTCL RLTVDKSRWQ	SCKASGYTFT TVDKSTSTAY SSASTKGPSV GVHTFPAVLQ ESKYGPPCPP EDPEVQFNWY YKCKVSNKGL VKGFYPSDIA EGNVFSCSVM	DNYMIWVRQA MELSSLRSED FPLAPCSRST SSGLYSLSV CPAPEFLGGP VDGVEVHNAK PSSIEKTISK VEWESNGQPE HEALHNHYTQ	PGQGLEWMGD TAVYYCARES SESTAALGCL VTVPSSSLGT SVFLFPPKPK TKPREEQFNS AKGQPREPQV NNYKTPPVVL KSLSLSLGK
55 h0301-H2 heavy chain	QVQLVQSGAE INPYNGGTTF PYFSNLYVMD VKDYFPEPVT KTYTCNVNDHK DTLMISRTP TYRVVSVLTV YTLPPSQEEM DSDGSFFLYS	VKKPGSSVKV NQKFKGRATL YWGQGTLLTV VSWNSGALTS PSNTKVDKRV VTCVVVDVSQ LHQDWLNGKE TKNQVSLTCL RLTVDKSRWQ	SCKASGYTFT TVDKSTSTAY SSASTKGPSV GVHTFPAVLQ ESKYGPPCPP EDPEVQFNWY YKCKVSNKGL VKGFYPSDIA EGNVFSCSVM	DNYMIWVRQA MELSSLRSED FPLAPCSRST SSGLYSLSV CPAPEFLGGP VDGVEVHNAK PSSIEKTISK VEWESNGQPE HEALHNHYTQ	PGQGLEWIGD TAVYYCARES SESTAALGCL VTVPSSSLGT SVFLFPPKPK TKPREEQFNS AKGQPREPQV NNYKTPPVVL KSLSLSLGK
56 H0302-H1 heavy chain	QVQLVQSGAE INPYTDVTY DGTFDYALDY KDYFPEPVT TYTCNVNDHKP TLMISRTP YRVVSVLTVL TLPPSQEEMT SDGSFFLYSR	VKKPGSSVKV NEKFKGRVTI WGQGTLLTVS SWNSGALTSG SNTKVDKRV TCVVVDVSQ HQDWLNGKEY KNQVSLTCLV LTVDKSRWQ	SCKASGYTFS TSDKSTSTAY SASTKGPSVF VHTFPAVLQS SKYGPPCPPC DPEVQFNWYV KCKVSNKGLP KGFPYSDIAV GNVFSCSVMH	DFNIHWVRQA MELSSLRSED PLAPCSRSTS SGLYSLSVV PAPEFLGGPS DGVEVHNAKT SSIEKTISKA EWESNGQPEN EALHNHYTQK	PGQGLEWMGY TAVYYCASYF ESTAALGCLV TVPSSSLGTK VFLFPPKPKD KPREEQFNST KGQPREPQVY NYKTPPVLD SLSLSLGK
57 H0302-H2 heavy chain	QVQLVQSGAE INPYTDVTY DGTFDYALDY KDYFPEPVT TYTCNVNDHKP TLMISRTP YRVVSVLTVL TLPPSQEEMT SDGSFFLYSR	VKKPGSSVKV NEKFKGRATL WGQGTLLTVS SWNSGALTSG SNTKVDKRV TCVVVDVSQ HQDWLNGKEY KNQVSLTCLV LTVDKSRWQ	SCKASGYTFS TSDKSTSTAY SASTKGPSVF VHTFPAVLQS SKYGPPCPPC DPEVQFNWYV KCKVSNKGLP KGFPYSDIAV GNVFSCSVMH	DFNIHWVRQA MELSSLRSED PLAPCSRSTS SGLYSLSVV PAPEFLGGPS DGVEVHNAKT SSIEKTISKA EWESNGQPEN EALHNHYTQK	PGQGLEWIGY TAVYYCASYF ESTAALGCLV TVPSSSLGTK VFLFPPKPKD KPREEQFNST KGQPREPQVY NYKTPPVLD SLSLSLGK
58 H0311-H1 heavy chain	QVQLVQSGAE INPNNGVVVY YHSNFGWYFD	VKKPGSSVKV NQKFKGRVTI SWGQGTLLTV	SCKASGYIFT TVDKSTSTAY SSASTKGPSV	DYNMHWVRQA MELSSLRSED FPLAPCSRST	PGQGLEWMGE TAVYYCTRAL SESTAALGCL

TABLE 8-continued

Sequences and Descriptions					
SEQ ID NO Description	Sequence				
	VKDYFPPEPVT	VSWNSGALTS	GVHTFPAVLQ	SSGLYSLSSV	VTVPSSSLGT
	KTYTCNVDPK	PSNTKVDKRV	ESKYGPCCPP	CPAPEFLGGP	SVFLFPPKPK
	DTLMISRTP	VTCVVVDVSQ	EDPEVQFNWY	VDGVEVHNAK	TKPREEQFNS
	TYRVVSVLTV	LHQDWLNGKE	YKCKVSNKGL	PSSIEKTISK	AKGQPREPQV
	YTLPPSQEEM	TKNQVSLTCL	VKGFYPSDIA	VEWESNGQPE	NNYKTPPV
	DSLDSGFFLYS	RLTVDKSRWQ	EGNVFSCSVM	HEALHNHYTQ	KSLSLSLGK
59 H0311-H2 heavy chain	QVQLVQSGAE	VKKPGSSVKV	SCKASGYIFT	DYNMHWVRQA	PGQGLEWMGE
	INPNNGVVVY	NQKFKGTTL	TVDKSTSTAY	MELSSLRSED	TAVYYCTRAL
	YHSNFGWYFD	SWGQGTTLTV	SSASTKGPSV	FPLAPCSRST	SESTAALGCL
	VKDYFPPEPVT	VSWNSGALTS	GVHTFPAVLQ	SSGLYSLSSV	VTVPSSSLGT
	KTYTCNVDPK	PSNTKVDKRV	ESKYGPCCPP	CPAPEFLGGP	SVFLFPPKPK
	DTLMISRTP	VTCVVVDVSQ	EDPEVQFNWY	VDGVEVHNAK	TKPREEQFNS
	TYRVVSVLTV	LHQDWLNGKE	YKCKVSNKGL	PSSIEKTISK	AKGQPREPQV
	YTLPPSQEEM	TKNQVSLTCL	VKGFYPSDIA	VEWESNGQPE	NNYKTPPV
	DSLDSGFFLYS	RLTVDKSRWQ	EGNVFSCSVM	HEALHNHYTQ	KSLSLSLGK
60 h0301-L0 light chain	EIVLTQSPAT	LSLSPGERAT	LSCKASQSVD	YDGDNYMNWY	QOKPGQAPRL
	LIYAASNLES	GIPARFSGSG	SGTDFTLTIS	SLEPEDFAVY	YCHLSNEDLS
	TFGGGTKEI	KRTVAAPSVF	IFPPSDEQLK	SGTASVVCCL	NNFYPREAKV
	QWKVDNALQS	GNSQESVTEQ	DSKDYSTYLS	STLTLSKADY	EKHKVYACEV
	THQGLSSPVT	KSFNRGEC			
61 h0301-L1 light chain	NIVLTQSPAT	LSLSPGERAT	LSCKASQSVD	YDGDNYMNWY	QOKPGQAPRL
	LIYAASNLES	GIPARFSGSG	SGTDFTLTIS	SLEPEDFAVY	YCHLSNEDLS
	TFGGGTKEI	KRTVAAPSVF	IFPPSDEQLK	SGTASVVCCL	NNFYPREAKV
	QWKVDNALQS	GNSQESVTEQ	DSKDYSTYLS	STLTLSKADY	EKHKVYACEV
	THQGLSSPVT	KSFNRGEC			
62 H0302-L0 light chain	EIVLTQSPAT	LSLSPGERAT	LSCRASESVD	NYGLSFMNMY	QOKPGQAPRL
	LIYTASNLES	GIPARFSGSG	SGTDFTLTIS	SLEPEDFAVY	YCQQSKELPW
	TFGGGTKEI	KRTVAAPSVF	IFPPSDEQLK	SGTASVVCCL	NNFYPREAKV
	QWKVDNALQS	GNSQESVTEQ	DSKDYSTYLS	STLTLSKADY	EKHKVYACEV
	THQGLSSPVT	KSFNRGEC			
63 H0302-L1 light chain	EIVLTQSPAT	LSLSPGERAT	LSCRASESVD	NYGLSFMNMY	QOKPGQAPRL
	LIYTASNLES	GIPARFSGSG	SGTDFTLTIS	SLEPEDFAVY	YCQQSKELPW
	TFGGGTKEI	KRTVAAPSVF	IFPPSDEQLK	SGTASVVCCL	NNFYPREAKV
	QWKVDNALQS	GNSQESVTEQ	DSKDYSTYLS	STLTLSKADY	EKHKVYACEV
	THQGLSSPVT	KSFNRGEC			
64 H0302-L2 light chain	EIVVTQSPAT	LSLSPGERAT	LSCRASESVD	NYGLSFMNWF	QOKPGQAPRL
	LIYTASNLES	GIPARFSGSG	SGTDFTLTIS	SLEPEDFAVY	YCQQSKELPW
	TFGGGTKEI	KRTVAAPSVF	IFPPSDEQLK	SGTASVVCCL	NNFYPREAKV
	QWKVDNALQS	GNSQESVTEQ	DSKDYSTYLS	STLTLSKADY	EKHKVYACEV
	THQGLSSPVT	KSFNRGEC			
65 H0311-L0 light chain	EIVLTQSPAT	LSLSPGERAT	LSCKASQSVD	YDGDHNMWY	QOKPGQAPRL
	LIYTASNLES	GIPARFSGSG	SGTDFTLTIS	SLEPEDFAVY	YCQQGNEDPW
	TFGGGTKEI	KRTVAAPSVF	IFPPSDEQLK	SGTASVVCCL	NNFYPREAKV
	QWKVDNALQS	GNSQESVTEQ	DSKDYSTYLS	STLTLSKADY	EKHKVYACEV
	THQGLSSPVT	KSFNRGEC			
66 H0311-L1 light chain	DIVLTQSPAT	LSLSPGERAT	LSCKASQSVD	YDGDHNMWY	QOKPGQAPRL
	LIYTASNLES	GIPARFSGSG	SGADFTLTIS	SLEPEDFAVY	YCQQGNEDPW
	TFGGGTKEI	KRTVAAPSVF	IFPPSDEQLK	SGTASVVCCL	NNFYPREAKV
	QWKVDNALQS	GNSQESVTEQ	DSKDYSTYLS	STLTLSKADY	EKHKVYACEV
	THQGLSSPVT	KSFNRGEC			
67 Human CSF1	EEVSEYCSHM	IGSGHLQSLQ	RLIDSQMETS	CQITFEFVDQ	EQLKDPVCYL
	KKAFLLVQDI	MEDTMRFRDN	TPNAIAIVQL	QELSLRLKSC	FTKDYEEHDK
	ACVRTFYETP	LQLLEKVKNV	FNETKNLLDK	DWNIFSKNCN	NSFAECSSQG
	HERQSEGS				
68 Human IL34	NEPLEMWPLT	QNEECTVTGF	LRDKLQYRSR	LQYMKHYFPI	NYKISVPYEG
	VFRIANVTRL	QRAQVSEREL	RYLWVLVLSATESVQDVL	EGHPSWKYLQ	
	EVQTLNLLNVQ	QGLTDVEVSP	KVESVLSLLN	APGPNLKLVR	PKALLDNCFR
	VMELLYCSCC	KQSSVLNWQD	CEVPSQSCS	PEPSLQYAAT	QLYPPPPWSP
	SSPPHSTGSV	RPVRAQGEGL	LP		

TABLE 8-continued

Sequences and Descriptions		
SEQ ID NO	Description	Sequence
69	Human acceptor A FR1	QVQLVQSGAE VKKPGSSVKV SCKAS
70	Human acceptor A FR2	WVRQAPGQGL EWMG
71	Human acceptor A FR3	RVTITADKST STAYMELSSL RSEDVAVYYC AR
72	Human acceptor A FR4	WGQGTLLTVS S
73	Human acceptor B FR1	QVQLVQSGAE VKKPGSSVKV SCKAS
74	Human acceptor B FR2	WVRQAPGQGL EWMG
75	Human acceptor B FR3	RVTITADKST STAYMELSSL RSEDVAVYYC AR
76	Human acceptor B FR4	WGQGTLLTVSS
77	Human acceptor C FR1	QVQLVQSGAE VKKPGSSVKV SCKAS
78	Human acceptor C FR2	WVRQAPGQGL EWMG
79	Human acceptor C FR3	RVTITADKST STAYMELSSL RSEDVAVYYC AR
80	Human acceptor C FR4	WGQGTLLTVS S
81	Human acceptor D FR1	EIVLTQSPAT LSLSPGERAT LSC
82	Human acceptor D FR2	WYQQKPGQAP RLLIY
83	Human acceptor D FR3	GIPARFSGSG SGTDFTLTIS SLEPEDFAVY YC
84	Human acceptor D FR4	FGGGTKVEIK
85	Human acceptor E FR1	EIVLTQSPAT LSLSPGERAT LSC
86	Human acceptor E FR2	WYQQKPGQAP RLLIY

TABLE 8-continued

Sequences and Descriptions	
SEQ ID NO	Description Sequence
87	Human acceptor E FR3 GIPARFSGSG SGTDFTLTIS SLEPEDFAVY YC
88	Human acceptor E FR4 FGQGTKVEIK
89	Human acceptor F FR1 EIVLTQSPAT LSLSPGERAT LSC
90	Human acceptor F FR2 WYQQKPGQAP RLLIY
91	Human acceptor F FR3 GIPARFSGSG SGTDFTLTIS SLEPEDFAVY YC
92	Human acceptor F FR4 FGQGTKVEIK
93	mCSF1R ECD-Fc APVIEPSGPE LVVEPGETVT LRCVSNGSVE WDGPISPYWT LDPESPGSTL TTRNATFKNT GTYRCTELED PMAGSTTIHL YVKDPAHSWN LLAQEVTVVE GQEAVLPLCI TDPALKDSVS LMREGGRQVL RKTVYFFSPW RGFIIRKAKV LDSNTYVCKT MVNGRESTST GIWLKVNVRH PEPPQIKLEP SKLVRIRGEA AQIVCSATNA EVGFNVILKR GDTKLEIPLN SDFQDNYYKK VRALSLNAVD FQDAGIYSCV ASNDVGTRTA TMNFQVVESA YLNLTSQSL LQEVSVGDSL ILTVHADAYP SIQHYNWYTL GPFFEDQRKL EFITQRAIYR YTFKLFLNRV KASEAGQYFL MAQNKAGWNN LTFELTLRYP PEVSVTWMPV NGSDVLFCDV SGYPQPSVTW MECRGHTDRC DEQAALQVWN DTHPEVLSQK PFDKVIIQSQ LPIGTLKHNM TYFCKTHNSV GNSSQYFRAV SLGQSKQEPK SSDKTHTCP CPAPELLGGP SVFLFPPKPK DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAK TKPREEQYNS TYRVVSVLTV LHQDWLNGKE YKCKVSNKAL PAPIEKTISK AKGQPREPQV YTLPPSRDEL TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTPPVVL DSDGSFFLYS KLTVDKSRWQ QGNVFSCSV HEALHNHYTQ KSLSLSPGK
94	Human IgG4 S241P ASTKGPSVFP LAPCSRSTSE STAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTKT YTCNVDHKPS NTKVDRVES KYGPPCPPCP APEFLGGPSV FLPPPKPKDT LMISRTPEVT CVVVDVSQED PEVQNWYVD GVEVHNAKTK PREEQFNSTY RVVSVLTVLH QDWLNGKEYK CKVSNKGLPS SIEKTISKAK GQPREPQVYT LPQSQEEMTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTPPVLDL DGSFFLYSRL TVDKSRWQEG NVFSCSVMH EALHNHYTQKS LSLSLGK
95	Human Igk RTVAAPSFI FPPSDEQLKS GTASVVCLLN NFYPREAKVQ WKVDNALQSG NSQESVTEQD SKDSTYLSL TLTLKADYE HKKVYACEVT HQGLSSPVTK SFNRGEC

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 95

<210> SEQ ID NO 1

<211> LENGTH: 953

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(953)

<223> OTHER INFORMATION: hCSF1R (full-length, no leader sequence)

<400> SEQUENCE: 1

Ile Pro Val Ile Glu Pro Ser Val Pro Glu Leu Val Val Lys Pro Gly

-continued

1	5	10	15
Ala Thr Val Thr Leu Arg Cys Val Gly Asn Gly Ser Val Glu Trp Asp	20	25	30
Gly Pro Pro Ser Pro His Trp Thr Leu Tyr Ser Asp Gly Ser Ser Ser	35	40	45
Ile Leu Ser Thr Asn Asn Ala Thr Phe Gln Asn Thr Gly Thr Tyr Arg	50	55	60
Cys Thr Glu Pro Gly Asp Pro Leu Gly Gly Ser Ala Ala Ile His Leu	65	70	80
Tyr Val Lys Asp Pro Ala Arg Pro Trp Asn Val Leu Ala Gln Glu Val	85	90	95
Val Val Phe Glu Asp Gln Asp Ala Leu Leu Pro Cys Leu Leu Thr Asp	100	105	110
Pro Val Leu Glu Ala Gly Val Ser Leu Val Arg Val Arg Gly Arg Pro	115	120	125
Leu Met Arg His Thr Asn Tyr Ser Phe Ser Pro Trp His Gly Phe Thr	130	135	140
Ile His Arg Ala Lys Phe Ile Gln Ser Gln Asp Tyr Gln Cys Ser Ala	145	150	155
Leu Met Gly Gly Arg Lys Val Met Ser Ile Ser Ile Arg Leu Lys Val	165	170	175
Gln Lys Val Ile Pro Gly Pro Pro Ala Leu Thr Leu Val Pro Ala Glu	180	185	190
Leu Val Arg Ile Arg Gly Glu Ala Ala Gln Ile Val Cys Ser Ala Ser	195	200	205
Ser Val Asp Val Asn Phe Asp Val Phe Leu Gln His Asn Asn Thr Lys	210	215	220
Leu Ala Ile Pro Gln Gln Ser Asp Phe His Asn Asn Arg Tyr Gln Lys	225	230	235
Val Leu Thr Leu Asn Leu Asp Gln Val Asp Phe Gln His Ala Gly Asn	245	250	255
Tyr Ser Cys Val Ala Ser Asn Val Gln Gly Lys His Ser Thr Ser Met	260	265	270
Phe Phe Arg Val Val Glu Ser Ala Tyr Leu Asn Leu Ser Ser Glu Gln	275	280	285
Asn Leu Ile Gln Glu Val Thr Val Gly Glu Gly Leu Asn Leu Lys Val	290	295	300
Met Val Glu Ala Tyr Pro Gly Leu Gln Gly Phe Asn Trp Thr Tyr Leu	305	310	315
Gly Pro Phe Ser Asp His Gln Pro Glu Pro Lys Leu Ala Asn Ala Thr	325	330	335
Thr Lys Asp Thr Tyr Arg His Thr Phe Thr Leu Ser Leu Pro Arg Leu	340	345	350
Lys Pro Ser Glu Ala Gly Arg Tyr Ser Phe Leu Ala Arg Asn Pro Gly	355	360	365
Gly Trp Arg Ala Leu Thr Phe Glu Leu Thr Leu Arg Tyr Pro Pro Glu	370	375	380
Val Ser Val Ile Trp Thr Phe Ile Asn Gly Ser Gly Thr Leu Leu Cys	385	390	395
Ala Ala Ser Gly Tyr Pro Gln Pro Asn Val Thr Trp Leu Gln Cys Ser	405	410	415
Gly His Thr Asp Arg Cys Asp Glu Ala Gln Val Leu Gln Val Trp Asp	420	425	430

-continued

Asp	Pro	Tyr	Pro	Glu	Val	Leu	Ser	Gln	Glu	Pro	Phe	His	Lys	Val	Thr
	435						440					445			
Val	Gln	Ser	Leu	Leu	Thr	Val	Glu	Thr	Leu	Glu	His	Asn	Gln	Thr	Tyr
	450						455				460				
Glu	Cys	Arg	Ala	His	Asn	Ser	Val	Gly	Ser	Gly	Ser	Trp	Ala	Phe	Ile
465					470					475					480
Pro	Ile	Ser	Ala	Gly	Ala	His	Thr	His	Pro	Pro	Asp	Glu	Phe	Leu	Phe
			485						490					495	
Thr	Pro	Val	Val	Val	Ala	Cys	Met	Ser	Ile	Met	Ala	Leu	Leu	Leu	Leu
			500					505					510		
Leu	Leu	Leu	Leu	Leu	Leu	Tyr	Lys	Tyr	Lys	Gln	Lys	Pro	Lys	Tyr	Gln
	515						520					525			
Val	Arg	Trp	Lys	Ile	Ile	Glu	Ser	Tyr	Glu	Gly	Asn	Ser	Tyr	Thr	Phe
	530					535					540				
Ile	Asp	Pro	Thr	Gln	Leu	Pro	Tyr	Asn	Glu	Lys	Trp	Glu	Phe	Pro	Arg
545					550					555					560
Asn	Asn	Leu	Gln	Phe	Gly	Lys	Thr	Leu	Gly	Ala	Gly	Ala	Phe	Gly	Lys
				565					570					575	
Val	Val	Glu	Ala	Thr	Ala	Phe	Gly	Leu	Gly	Lys	Glu	Asp	Ala	Val	Leu
			580					585					590		
Lys	Val	Ala	Val	Lys	Met	Leu	Lys	Ser	Thr	Ala	His	Ala	Asp	Glu	Lys
	595					600						605			
Glu	Ala	Leu	Met	Ser	Glu	Leu	Lys	Ile	Met	Ser	His	Leu	Gly	Gln	His
	610					615					620				
Glu	Asn	Ile	Val	Asn	Leu	Leu	Gly	Ala	Cys	Thr	His	Gly	Gly	Pro	Val
625					630					635					640
Leu	Val	Ile	Thr	Glu	Tyr	Cys	Cys	Tyr	Gly	Asp	Leu	Leu	Asn	Phe	Leu
			645						650					655	
Arg	Arg	Lys	Ala	Glu	Ala	Met	Leu	Gly	Pro	Ser	Leu	Ser	Pro	Gly	Gln
			660					665					670		
Asp	Pro	Glu	Gly	Gly	Val	Asp	Tyr	Lys	Asn	Ile	His	Leu	Glu	Lys	Lys
	675					680						685			
Tyr	Val	Arg	Arg	Asp	Ser	Gly	Phe	Ser	Ser	Gln	Gly	Val	Asp	Thr	Tyr
	690					695					700				
Val	Glu	Met	Arg	Pro	Val	Ser	Thr	Ser	Ser	Asn	Asp	Ser	Phe	Ser	Glu
705					710					715					720
Gln	Asp	Leu	Asp	Lys	Glu	Asp	Gly	Arg	Pro	Leu	Glu	Leu	Arg	Asp	Leu
				725					730					735	
Leu	His	Phe	Ser	Ser	Gln	Val	Ala	Gln	Gly	Met	Ala	Phe	Leu	Ala	Ser
			740					745					750		
Lys	Asn	Cys	Ile	His	Arg	Asp	Val	Ala	Ala	Arg	Asn	Val	Leu	Leu	Thr
	755					760						765			
Asn	Gly	His	Val	Ala	Lys	Ile	Gly	Asp	Phe	Gly	Leu	Ala	Arg	Asp	Ile
	770				775						780				
Met	Asn	Asp	Ser	Asn	Tyr	Ile	Val	Lys	Gly	Asn	Ala	Arg	Leu	Pro	Val
785					790					795					800
Lys	Trp	Met	Ala	Pro	Glu	Ser	Ile	Phe	Asp	Cys	Val	Tyr	Thr	Val	Gln
				805					810					815	
Ser	Asp	Val	Trp	Ser	Tyr	Gly	Ile	Leu	Leu	Trp	Glu	Ile	Phe	Ser	Leu
			820					825					830		
Gly	Leu	Asn	Pro	Tyr	Pro	Gly	Ile	Leu	Val	Asn	Ser	Lys	Phe	Tyr	Lys
	835						840						845		

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Leu Val Lys Asp Gly Tyr Gln Met Ala Gln Pro Ala Phe Ala Pro Lys
 850                               855                               860

Asn Ile Tyr Ser Ile Met Gln Ala Cys Trp Ala Leu Glu Pro Thr His
865                               870                               875                               880

Arg Pro Thr Phe Gln Gln Ile Cys Ser Phe Leu Gln Glu Gln Ala Gln
                               885                               890                               895

Glu Asp Arg Arg Glu Arg Asp Tyr Thr Asn Leu Pro Ser Ser Ser Arg
                               900                               905                               910

Ser Gly Gly Ser Gly Ser Ser Ser Ser Glu Leu Glu Glu Glu Ser Ser
 915                               920                               925

Ser Glu His Leu Thr Cys Cys Glu Gln Gly Asp Ile Ala Gln Pro Leu
 930                               935                               940

Leu Gln Pro Asn Asn Tyr Gln Phe Cys
945                               950

```

```

<210> SEQ ID NO 2
<211> LENGTH: 972
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(972)
<223> OTHER INFORMATION: hCSF1R (full-length, + leader sequence)

```

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<400> SEQUENCE: 2

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```

Met Gly Pro Gly Val Leu Leu Leu Leu Val Ala Thr Ala Trp His
 1                               5                               10                               15

Gly Gln Gly Ile Pro Val Ile Glu Pro Ser Val Pro Glu Leu Val Val
 20                               25                               30

Lys Pro Gly Ala Thr Val Thr Leu Arg Cys Val Gly Asn Gly Ser Val
 35                               40                               45

Glu Trp Asp Gly Pro Pro Ser Pro His Trp Thr Leu Tyr Ser Asp Gly
 50                               55                               60

Ser Ser Ser Ile Leu Ser Thr Asn Asn Ala Thr Phe Gln Asn Thr Gly
 65                               70                               75                               80

Thr Tyr Arg Cys Thr Glu Pro Gly Asp Pro Leu Gly Gly Ser Ala Ala
 85                               90                               95

Ile His Leu Tyr Val Lys Asp Pro Ala Arg Pro Trp Asn Val Leu Ala
 100                              105                              110

Gln Glu Val Val Val Phe Glu Asp Gln Asp Ala Leu Leu Pro Cys Leu
 115                              120                              125

Leu Thr Asp Pro Val Leu Glu Ala Gly Val Ser Leu Val Arg Val Arg
 130                              135                              140

Gly Arg Pro Leu Met Arg His Thr Asn Tyr Ser Phe Ser Pro Trp His
 145                              150                              155                              160

Gly Phe Thr Ile His Arg Ala Lys Phe Ile Gln Ser Gln Asp Tyr Gln
 165                              170                              175

Cys Ser Ala Leu Met Gly Gly Arg Lys Val Met Ser Ile Ser Ile Arg
 180                              185                              190

Leu Lys Val Gln Lys Val Ile Pro Gly Pro Pro Ala Leu Thr Leu Val
 195                              200                              205

Pro Ala Glu Leu Val Arg Ile Arg Gly Glu Ala Ala Gln Ile Val Cys
 210                              215                              220

Ser Ala Ser Ser Val Asp Val Asn Phe Asp Val Phe Leu Gln His Asn
 225                              230                              235                              240

Asn Thr Lys Leu Ala Ile Pro Gln Gln Ser Asp Phe His Asn Asn Arg

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245								250					255				
Tyr	Gln	Lys	Val	Leu	Thr	Leu	Asn	Leu	Asp	Gln	Val	Asp	Phe	Gln	His		
			260					265					270				
Ala	Gly	Asn	Tyr	Ser	Cys	Val	Ala	Ser	Asn	Val	Gln	Gly	Lys	His	Ser		
			275				280					285					
Thr	Ser	Met	Phe	Phe	Arg	Val	Val	Glu	Ser	Ala	Tyr	Leu	Asn	Leu	Ser		
			290			295					300						
Ser	Glu	Gln	Asn	Leu	Ile	Gln	Glu	Val	Thr	Val	Gly	Glu	Gly	Leu	Asn		
305					310					315				320			
Leu	Lys	Val	Met	Val	Glu	Ala	Tyr	Pro	Gly	Leu	Gln	Gly	Phe	Asn	Trp		
				325					330					335			
Thr	Tyr	Leu	Gly	Pro	Phe	Ser	Asp	His	Gln	Pro	Glu	Pro	Lys	Leu	Ala		
			340					345					350				
Asn	Ala	Thr	Thr	Lys	Asp	Thr	Tyr	Arg	His	Thr	Phe	Thr	Leu	Ser	Leu		
			355					360				365					
Pro	Arg	Leu	Lys	Pro	Ser	Glu	Ala	Gly	Arg	Tyr	Ser	Phe	Leu	Ala	Arg		
						375					380						
Asn	Pro	Gly	Gly	Trp	Arg	Ala	Leu	Thr	Phe	Glu	Leu	Thr	Leu	Arg	Tyr		
385					390					395				400			
Pro	Pro	Glu	Val	Ser	Val	Ile	Trp	Thr	Phe	Ile	Asn	Gly	Ser	Gly	Thr		
				405					410					415			
Leu	Leu	Cys	Ala	Ala	Ser	Gly	Tyr	Pro	Gln	Pro	Asn	Val	Thr	Trp	Leu		
			420					425					430				
Gln	Cys	Ser	Gly	His	Thr	Asp	Arg	Cys	Asp	Glu	Ala	Gln	Val	Leu	Gln		
			435				440					445					
Val	Trp	Asp	Asp	Pro	Tyr	Pro	Glu	Val	Leu	Ser	Gln	Glu	Pro	Phe	His		
			450			455						460					
Lys	Val	Thr	Val	Gln	Ser	Leu	Leu	Thr	Val	Glu	Thr	Leu	Glu	His	Asn		
465					470					475				480			
Gln	Thr	Tyr	Glu	Cys	Arg	Ala	His	Asn	Ser	Val	Gly	Ser	Gly	Ser	Trp		
				485					490					495			
Ala	Phe	Ile	Pro	Ile	Ser	Ala	Gly	Ala	His	Thr	His	Pro	Pro	Asp	Glu		
			500					505						510			
Phe	Leu	Phe	Thr	Pro	Val	Val	Val	Ala	Cys	Met	Ser	Ile	Met	Ala	Leu		
			515					520				525					
Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Tyr	Lys	Tyr	Lys	Gln	Lys	Pro		
			530			535					540						
Lys	Tyr	Gln	Val	Arg	Trp	Lys	Ile	Ile	Glu	Ser	Tyr	Glu	Gly	Asn	Ser		
545					550					555				560			
Tyr	Thr	Phe	Ile	Asp	Pro	Thr	Gln	Leu	Pro	Tyr	Asn	Glu	Lys	Trp	Glu		
				565					570					575			
Phe	Pro	Arg	Asn	Asn	Leu	Gln	Phe	Gly	Lys	Thr	Leu	Gly	Ala	Gly	Ala		
			580					585					590				
Phe	Gly	Lys	Val	Val	Glu	Ala	Thr	Ala	Phe	Gly	Leu	Gly	Lys	Glu	Asp		
			595				600					605					
Ala	Val	Leu	Lys	Val	Ala	Val	Lys	Met	Leu	Lys	Ser	Thr	Ala	His	Ala		
			610			615					620						
Asp	Glu	Lys	Glu	Ala	Leu	Met	Ser	Glu	Leu	Lys	Ile	Met	Ser	His	Leu		
625					630					635				640			
Gly	Gln	His	Glu	Asn	Ile	Val	Asn	Leu	Leu	Gly	Ala	Cys	Thr	His	Gly		
				645					650					655			
Gly	Pro	Val	Leu	Val	Ile	Thr	Glu	Tyr	Cys	Cys	Tyr	Gly	Asp	Leu	Leu		
			660					665					670				

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Asn Phe Leu Arg Arg Lys Ala Glu Ala Met Leu Gly Pro Ser Leu Ser
   675                               680                               685

Pro Gly Gln Asp Pro Glu Gly Gly Val Asp Tyr Lys Asn Ile His Leu
   690                               695                               700

Glu Lys Lys Tyr Val Arg Arg Asp Ser Gly Phe Ser Ser Gln Gly Val
   705                               710                               715                               720

Asp Thr Tyr Val Glu Met Arg Pro Val Ser Thr Ser Ser Asn Asp Ser
   725                               730                               735

Phe Ser Glu Gln Asp Leu Asp Lys Glu Asp Gly Arg Pro Leu Glu Leu
   740                               745                               750

Arg Asp Leu Leu His Phe Ser Ser Gln Val Ala Gln Gly Met Ala Phe
   755                               760                               765

Leu Ala Ser Lys Asn Cys Ile His Arg Asp Val Ala Ala Arg Asn Val
   770                               775                               780

Leu Leu Thr Asn Gly His Val Ala Lys Ile Gly Asp Phe Gly Leu Ala
   785                               790                               795                               800

Arg Asp Ile Met Asn Asp Ser Asn Tyr Ile Val Lys Gly Asn Ala Arg
   805                               810                               815

Leu Pro Val Lys Trp Met Ala Pro Glu Ser Ile Phe Asp Cys Val Tyr
   820                               825                               830

Thr Val Gln Ser Asp Val Trp Ser Tyr Gly Ile Leu Leu Trp Glu Ile
   835                               840                               845

Phe Ser Leu Gly Leu Asn Pro Tyr Pro Gly Ile Leu Val Asn Ser Lys
   850                               855                               860

Phe Tyr Lys Leu Val Lys Asp Gly Tyr Gln Met Ala Gln Pro Ala Phe
   865                               870                               875                               880

Ala Pro Lys Asn Ile Tyr Ser Ile Met Gln Ala Cys Trp Ala Leu Glu
   885                               890                               895

Pro Thr His Arg Pro Thr Phe Gln Gln Ile Cys Ser Phe Leu Gln Glu
   900                               905                               910

Gln Ala Gln Glu Asp Arg Arg Glu Arg Asp Tyr Thr Asn Leu Pro Ser
   915                               920                               925

Ser Ser Arg Ser Gly Gly Ser Gly Ser Ser Ser Ser Glu Leu Glu Glu
   930                               935                               940

Glu Ser Ser Ser Glu His Leu Thr Cys Cys Glu Gln Gly Asp Ile Ala
   945                               950                               955                               960

Gln Pro Leu Leu Gln Pro Asn Asn Tyr Gln Phe Cys
   965                               970

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```

<210> SEQ ID NO 3
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(20)
<223> OTHER INFORMATION: Light chain leader sequence

```

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<400> SEQUENCE: 3

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```

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1             5             10             15

Gly Ser Thr Gly
           20

```

```

<210> SEQ ID NO 4
<211> LENGTH: 19

```

-continued

```

<212> TYPE: PRT
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(19)
<223> OTHER INFORMATION: Heavy chain leader sequence

<400> SEQUENCE: 4

Met Ala Val Leu Gly Leu Leu Leu Cys Leu Val Thr Phe Pro Ser Cys
1             5             10             15

Val Leu Ser

<210> SEQ ID NO 5
<211> LENGTH: 487
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(487)
<223> OTHER INFORMATION: hCSF1R ECD.506

<400> SEQUENCE: 5

Ile Pro Val Ile Glu Pro Ser Val Pro Glu Leu Val Val Lys Pro Gly
1             5             10             15

Ala Thr Val Thr Leu Arg Cys Val Gly Asn Gly Ser Val Glu Trp Asp
20            25            30

Gly Pro Pro Ser Pro His Trp Thr Leu Tyr Ser Asp Gly Ser Ser Ser
35            40            45

Ile Leu Ser Thr Asn Asn Ala Thr Phe Gln Asn Thr Gly Thr Tyr Arg
50            55            60

Cys Thr Glu Pro Gly Asp Pro Leu Gly Gly Ser Ala Ala Ile His Leu
65            70            75            80

Tyr Val Lys Asp Pro Ala Arg Pro Trp Asn Val Leu Ala Gln Glu Val
85            90            95

Val Val Phe Glu Asp Gln Asp Ala Leu Leu Pro Cys Leu Leu Thr Asp
100           105           110

Pro Val Leu Glu Ala Gly Val Ser Leu Val Arg Val Arg Gly Arg Pro
115           120           125

Leu Met Arg His Thr Asn Tyr Ser Phe Ser Pro Trp His Gly Phe Thr
130           135           140

Ile His Arg Ala Lys Phe Ile Gln Ser Gln Asp Tyr Gln Cys Ser Ala
145           150           155           160

Leu Met Gly Gly Arg Lys Val Met Ser Ile Ser Ile Arg Leu Lys Val
165           170           175

Gln Lys Val Ile Pro Gly Pro Pro Ala Leu Thr Leu Val Pro Ala Glu
180           185           190

Leu Val Arg Ile Arg Gly Glu Ala Ala Gln Ile Val Cys Ser Ala Ser
195           200           205

Ser Val Asp Val Asn Phe Asp Val Phe Leu Gln His Asn Asn Thr Lys
210           215           220

Leu Ala Ile Pro Gln Gln Ser Asp Phe His Asn Asn Arg Tyr Gln Lys
225           230           235           240

Val Leu Thr Leu Asn Leu Asp Gln Val Asp Phe Gln His Ala Gly Asn
245           250           255

Tyr Ser Cys Val Ala Ser Asn Val Gln Gly Lys His Ser Thr Ser Met
260           265           270

Phe Phe Arg Val Val Glu Ser Ala Tyr Leu Asn Leu Ser Ser Glu Gln
275           280           285

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Asn Leu Ile Gln Glu Val Thr Val Gly Glu Gly Leu Asn Leu Lys Val
290                295                300

Met Val Glu Ala Tyr Pro Gly Leu Gln Gly Phe Asn Trp Thr Tyr Leu
305                310                315                320

Gly Pro Phe Ser Asp His Gln Pro Glu Pro Lys Leu Ala Asn Ala Thr
                325                330                335

Thr Lys Asp Thr Tyr Arg His Thr Phe Thr Leu Ser Leu Pro Arg Leu
                340                345                350

Lys Pro Ser Glu Ala Gly Arg Tyr Ser Phe Leu Ala Arg Asn Pro Gly
                355                360                365

Gly Trp Arg Ala Leu Thr Phe Glu Leu Thr Leu Arg Tyr Pro Pro Glu
370                375                380

Val Ser Val Ile Trp Thr Phe Ile Asn Gly Ser Gly Thr Leu Leu Cys
385                390                395                400

Ala Ala Ser Gly Tyr Pro Gln Pro Asn Val Thr Trp Leu Gln Cys Ser
                405                410                415

Gly His Thr Asp Arg Cys Asp Glu Ala Gln Val Leu Gln Val Trp Asp
                420                425                430

Asp Pro Tyr Pro Glu Val Leu Ser Gln Glu Pro Phe His Lys Val Thr
                435                440                445

Val Gln Ser Leu Leu Thr Val Glu Thr Leu Glu His Asn Gln Thr Tyr
450                455                460

Glu Cys Arg Ala His Asn Ser Val Gly Ser Gly Ser Trp Ala Phe Ile
465                470                475                480

Pro Ile Ser Ala Gly Ala His
                485

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```

<210> SEQ ID NO 6
<211> LENGTH: 719
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(719)
<223> OTHER INFORMATION: hCSF1R ECD.506-Fc

```

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<400> SEQUENCE: 6

```

```

Ile Pro Val Ile Glu Pro Ser Val Pro Glu Leu Val Val Lys Pro Gly
1                5                10                15

Ala Thr Val Thr Leu Arg Cys Val Gly Asn Gly Ser Val Glu Trp Asp
                20                25                30

Gly Pro Pro Ser Pro His Trp Thr Leu Tyr Ser Asp Gly Ser Ser Ser
                35                40                45

Ile Leu Ser Thr Asn Asn Ala Thr Phe Gln Asn Thr Gly Thr Tyr Arg
50                55                60

Cys Thr Glu Pro Gly Asp Pro Leu Gly Gly Ser Ala Ala Ile His Leu
65                70                75                80

Tyr Val Lys Asp Pro Ala Arg Pro Trp Asn Val Leu Ala Gln Glu Val
                85                90                95

Val Val Phe Glu Asp Gln Asp Ala Leu Leu Pro Cys Leu Leu Thr Asp
                100                105                110

Pro Val Leu Glu Ala Gly Val Ser Leu Val Arg Val Arg Gly Arg Pro
                115                120                125

Leu Met Arg His Thr Asn Tyr Ser Phe Ser Pro Trp His Gly Phe Thr
130                135                140

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Ile	His	Arg	Ala	Lys	Phe	Ile	Gln	Ser	Gln	Asp	Tyr	Gln	Cys	Ser	Ala	145	150	155	160
Leu	Met	Gly	Gly	Arg	Lys	Val	Met	Ser	Ile	Ser	Ile	Arg	Leu	Lys	Val	165	170	175	
Gln	Lys	Val	Ile	Pro	Gly	Pro	Pro	Ala	Leu	Thr	Leu	Val	Pro	Ala	Glu	180	185	190	
Leu	Val	Arg	Ile	Arg	Gly	Glu	Ala	Ala	Gln	Ile	Val	Cys	Ser	Ala	Ser	195	200	205	
Ser	Val	Asp	Val	Asn	Phe	Asp	Val	Phe	Leu	Gln	His	Asn	Asn	Thr	Lys	210	215	220	
Leu	Ala	Ile	Pro	Gln	Gln	Ser	Asp	Phe	His	Asn	Asn	Arg	Tyr	Gln	Lys	225	230	235	240
Val	Leu	Thr	Leu	Asn	Leu	Asp	Gln	Val	Asp	Phe	Gln	His	Ala	Gly	Asn	245	250	255	
Tyr	Ser	Cys	Val	Ala	Ser	Asn	Val	Gln	Gly	Lys	His	Ser	Thr	Ser	Met	260	265	270	
Phe	Phe	Arg	Val	Val	Glu	Ser	Ala	Tyr	Leu	Asn	Leu	Ser	Ser	Glu	Gln	275	280	285	
Asn	Leu	Ile	Gln	Glu	Val	Thr	Val	Gly	Glu	Gly	Leu	Asn	Leu	Lys	Val	290	295	300	
Met	Val	Glu	Ala	Tyr	Pro	Gly	Leu	Gln	Gly	Phe	Asn	Trp	Thr	Tyr	Leu	305	310	315	320
Gly	Pro	Phe	Ser	Asp	His	Gln	Pro	Glu	Pro	Lys	Leu	Ala	Asn	Ala	Thr	325	330	335	
Thr	Lys	Asp	Thr	Tyr	Arg	His	Thr	Phe	Thr	Leu	Ser	Leu	Pro	Arg	Leu	340	345	350	
Lys	Pro	Ser	Glu	Ala	Gly	Arg	Tyr	Ser	Phe	Leu	Ala	Arg	Asn	Pro	Gly	355	360	365	
Gly	Trp	Arg	Ala	Leu	Thr	Phe	Glu	Leu	Thr	Leu	Arg	Tyr	Pro	Pro	Glu	370	375	380	
Val	Ser	Val	Ile	Trp	Thr	Phe	Ile	Asn	Gly	Ser	Gly	Thr	Leu	Leu	Cys	385	390	395	400
Ala	Ala	Ser	Gly	Tyr	Pro	Gln	Pro	Asn	Val	Thr	Trp	Leu	Gln	Cys	Ser	405	410	415	
Gly	His	Thr	Asp	Arg	Cys	Asp	Glu	Ala	Gln	Val	Leu	Gln	Val	Trp	Asp	420	425	430	
Asp	Pro	Tyr	Pro	Glu	Val	Leu	Ser	Gln	Glu	Pro	Phe	His	Lys	Val	Thr	435	440	445	
Val	Gln	Ser	Leu	Leu	Thr	Val	Glu	Thr	Leu	Glu	His	Asn	Gln	Thr	Tyr	450	455	460	
Glu	Cys	Arg	Ala	His	Asn	Ser	Val	Gly	Ser	Gly	Ser	Trp	Ala	Phe	Ile	465	470	475	480
Pro	Ile	Ser	Ala	Gly	Ala	His	Glu	Pro	Lys	Ser	Ser	Asp	Lys	Thr	His	485	490	495	
Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	500	505	510	
Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	515	520	525	
Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	530	535	540	
Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	545	550	555	560
Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser				

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	565	570	575
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys	580	585	590
Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile	595	600	605
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro	610	615	620
Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu	625	630	635
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn	645	650	655
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser	660	665	670
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg	675	680	685
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu	690	695	700
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys	705	710	715
<210> SEQ ID NO 7			
<211> LENGTH: 506			
<212> TYPE: PRT			
<213> ORGANISM: Macaca cynomolgus			
<220> FEATURE:			
<221> NAME/KEY: misc_feature			
<222> LOCATION: (1) .. (506)			
<223> OTHER INFORMATION: cynoCSF1R ECD (with leader sequence)			
<400> SEQUENCE: 7			
Met Gly Pro Gly Val Leu Leu Leu Leu Val Val Thr Ala Trp His	1	5	10
Gly Gln Gly Ile Pro Val Ile Glu Pro Ser Gly Pro Glu Leu Val Val	20	25	30
Lys Pro Gly Glu Thr Val Thr Leu Arg Cys Val Gly Asn Gly Ser Val	35	40	45
Glu Trp Asp Gly Pro Ile Ser Pro His Trp Thr Leu Tyr Ser Asp Gly	50	55	60
Pro Ser Ser Val Leu Thr Thr Thr Asn Ala Thr Phe Gln Asn Thr Arg	65	70	75
Thr Tyr Arg Cys Thr Glu Pro Gly Asp Pro Leu Gly Gly Ser Ala Ala	85	90	95
Ile His Leu Tyr Val Lys Asp Pro Ala Arg Pro Trp Asn Val Leu Ala	100	105	110
Lys Glu Val Val Val Phe Glu Asp Gln Asp Ala Leu Leu Pro Cys Leu	115	120	125
Leu Thr Asp Pro Val Leu Glu Ala Gly Val Ser Leu Val Arg Leu Arg	130	135	140
Gly Arg Pro Leu Leu Arg His Thr Asn Tyr Ser Phe Ser Pro Trp His	145	150	155
Gly Phe Thr Ile His Arg Ala Lys Phe Ile Gln Gly Gln Asp Tyr Gln	165	170	175
Cys Ser Ala Leu Met Gly Ser Arg Lys Val Met Ser Ile Ser Ile Arg	180	185	190
Leu Lys Val Gln Lys Val Ile Pro Gly Pro Pro Ala Leu Thr Leu Val	195	200	205

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Pro Ala Glu Leu Val Arg Ile Arg Gly Glu Ala Ala Gln Ile Val Cys
 210                215                220

Ser Ala Ser Asn Ile Asp Val Asp Phe Asp Val Phe Leu Gln His Asn
225                230                235                240

Thr Thr Lys Leu Ala Ile Pro Gln Arg Ser Asp Phe His Asp Asn Arg
                245                250                255

Tyr Gln Lys Val Leu Thr Leu Ser Leu Gly Gln Val Asp Phe Gln His
                260                265                270

Ala Gly Asn Tyr Ser Cys Val Ala Ser Asn Val Gln Gly Lys His Ser
                275                280                285

Thr Ser Met Phe Phe Arg Val Val Glu Ser Ala Tyr Leu Asp Leu Ser
290                295                300

Ser Glu Gln Asn Leu Ile Gln Glu Val Thr Val Gly Glu Gly Leu Asn
305                310                315                320

Leu Lys Val Met Val Glu Ala Tyr Pro Gly Leu Gln Gly Phe Asn Trp
                325                330                335

Thr Tyr Leu Gly Pro Phe Ser Asp His Gln Pro Glu Pro Lys Leu Ala
                340                345                350

Asn Ala Thr Thr Lys Asp Thr Tyr Arg His Thr Phe Thr Leu Ser Leu
                355                360                365

Pro Arg Leu Lys Pro Ser Glu Ala Gly Arg Tyr Ser Phe Leu Ala Arg
370                375                380

Asn Pro Gly Gly Trp Arg Ala Leu Thr Phe Glu Leu Thr Leu Arg Tyr
385                390                395                400

Pro Pro Glu Val Ser Val Ile Trp Thr Ser Ile Asn Gly Ser Gly Thr
                405                410                415

Leu Leu Cys Ala Ala Ser Gly Tyr Pro Gln Pro Asn Val Thr Trp Leu
                420                425                430

Gln Cys Ala Gly His Thr Asp Arg Cys Asp Glu Ala Gln Val Leu Gln
                435                440                445

Val Trp Val Asp Pro His Pro Glu Val Leu Ser Gln Glu Pro Phe Gln
450                455                460

Lys Val Thr Val Gln Ser Leu Leu Thr Ala Glu Thr Leu Glu His Asn
465                470                475                480

Gln Thr Tyr Glu Cys Arg Ala His Asn Ser Val Gly Ser Gly Ser Trp
                485                490                495

Ala Phe Ile Pro Ile Ser Ala Gly Ala Arg
                500                505

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<210> SEQ ID NO 8
<211> LENGTH: 740
<212> TYPE: PRT
<213> ORGANISM: Macaca cynomolgus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(740)
<223> OTHER INFORMATION: cynoCSF1R ECD-Fc (with leader sequence)

<400> SEQUENCE: 8

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Met Gly Pro Gly Val Leu Leu Leu Leu Val Val Thr Ala Trp His
 1                5                10                15

Gly Gln Gly Ile Pro Val Ile Glu Pro Ser Gly Pro Glu Leu Val Val
                20                25                30

Lys Pro Gly Glu Thr Val Thr Leu Arg Cys Val Gly Asn Gly Ser Val
35                40                45

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Glu 50	Trp	Asp	Gly	Pro	Ile	Ser 55	Pro	His	Trp	Thr	Leu 60	Tyr	Ser	Asp	Gly
Pro 65	Ser	Ser	Val	Leu	Thr 70	Thr	Thr	Asn	Ala	Thr 75	Phe	Gln	Asn	Thr	Arg 80
Thr	Tyr	Arg	Cys 85	Thr	Glu	Pro	Gly	Asp 90	Pro	Leu	Gly	Gly	Ser	Ala 95	Ala
Ile	His	Leu	Tyr 100	Val	Lys	Asp	Pro	Ala 105	Arg	Pro	Trp	Asn	Val	Leu	Ala
Lys	Glu	Val	Val 115	Val	Phe	Glu	Asp 120	Gln	Asp	Ala	Leu	Leu 125	Pro	Cys	Leu
Leu	Thr 130	Asp	Pro	Val	Leu	Glu 135	Ala	Gly	Val	Ser	Leu 140	Val	Arg	Leu	Arg
Gly 145	Arg	Pro	Leu	Leu	Arg 150	His	Thr	Asn	Tyr	Ser 155	Phe	Ser	Pro	Trp	His 160
Gly	Phe	Thr	Ile 165	His	Arg	Ala	Lys	Phe	Ile 170	Gln	Gly	Gln	Asp	Tyr 175	Gln
Cys	Ser	Ala	Leu 180	Met	Gly	Ser	Arg	Lys 185	Val	Met	Ser	Ile	Ser	Ile	Arg
Leu	Lys 195	Val	Gln	Lys	Val	Ile	Pro 200	Gly	Pro	Pro	Ala	Leu 205	Thr	Leu	Val
Pro 210	Ala	Glu	Leu	Val	Arg	Ile 215	Arg	Gly	Glu	Ala	Ala 220	Gln	Ile	Val	Cys
Ser 225	Ala	Ser	Asn	Ile	Asp 230	Val	Asp	Phe	Asp	Val 235	Phe	Leu	Gln	His	Asn 240
Thr	Thr	Lys	Leu 245	Ala	Ile	Pro	Gln	Arg	Ser 250	Asp	Phe	His	Asp	Asn 255	Arg
Tyr	Gln	Lys	Val 260	Leu	Thr	Leu	Ser	Leu 265	Gly	Gln	Val	Asp	Phe	Gln	His
Ala	Gly 275	Asn	Tyr	Ser	Cys	Val	Ala 280	Ser	Asn	Val	Gln	Gly 285	Lys	His	Ser
Thr 290	Ser	Met	Phe	Phe	Arg	Val 295	Val	Glu	Ser	Ala	Tyr 300	Leu	Asp	Leu	Ser
Ser 305	Glu	Gln	Asn	Leu	Ile 310	Gln	Glu	Val	Thr	Val 315	Gly	Glu	Gly	Leu	Asn 320
Leu	Lys	Val	Met 325	Val	Glu	Ala	Tyr	Pro	Gly 330	Leu	Gln	Gly	Phe	Asn 335	Trp
Thr	Tyr	Leu	Gly 340	Pro	Phe	Ser	Asp	His 345	Gln	Pro	Glu	Pro	Lys 350	Leu	Ala
Asn	Ala 355	Thr	Thr	Lys	Asp	Thr	Tyr 360	Arg	His	Thr	Phe	Thr 365	Leu	Ser	Leu
Pro 370	Arg	Leu	Lys	Pro	Ser	Glu 375	Ala	Gly	Arg	Tyr	Ser 380	Phe	Leu	Ala	Arg
Asn 385	Pro	Gly	Gly	Trp	Arg 390	Ala	Leu	Thr	Phe	Glu 395	Leu	Thr	Leu	Arg	Tyr 400
Pro	Pro	Glu	Val 405	Ser	Val	Ile	Trp	Thr	Ser 410	Ile	Asn	Gly	Ser	Gly 415	Thr
Leu	Leu	Cys	Ala 420	Ala	Ser	Gly	Tyr	Pro	Gln	Pro	Asn	Val	Thr 430	Trp	Leu
Gln	Cys 435	Ala	Gly	His	Thr	Asp	Arg	Cys 440	Asp	Glu	Ala	Gln 445	Val	Leu	Gln
Val 450	Trp	Val	Asp	Pro	His	Pro 455	Glu	Val	Leu	Ser	Gln 460	Glu	Pro	Phe	Gln
Lys	Val	Thr	Val	Gln	Ser	Leu	Leu	Thr	Ala	Glu	Thr	Leu	Glu	His	Asn

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465	470	475	480
Gln Thr Tyr Glu Cys Arg Ala His Asn Ser Val Gly Ser Gly Ser Trp			
	485	490	495
Ala Phe Ile Pro Ile Ser Ala Gly Ala Arg Gly Ser Glu Pro Lys Ser			
	500	505	510
Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu			
	515	520	525
Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu			
	530	535	540
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser			
	545	550	555
His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu			
	565	570	575
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr			
	580	585	590
Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn			
	595	600	605
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro			
	610	615	620
Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln			
	625	630	635
Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val			
	645	650	655
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val			
	660	665	670
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro			
	675	680	685
Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr			
	690	695	700
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val			
	705	710	715
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu			
	725	730	735
Ser Pro Gly Lys			
	740		

<210> SEQ ID NO 9
 <211> LENGTH: 122
 <212> TYPE: PRT
 <213> ORGANISM: Mus musculus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1) .. (122)
 <223> OTHER INFORMATION: Fab 0301 heavy chain variable region

<400> SEQUENCE: 9

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Arg Pro Gly Ala			
1	5	10	15
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Asn			
	20	25	30
Tyr Met Ile Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile			
	35	40	45
Gly Asp Ile Asn Pro Tyr Asn Gly Gly Thr Thr Phe Asn Gln Lys Phe			
	50	55	60
Lys Gly Lys Ala Thr Leu Thr Val Glu Lys Ser Ser Ser Thr Ala Tyr			
	65	70	75
			80

Met	Gln	Leu	Asn	Ser	Leu	Thr	Ser	Glu	Asp	Ser	Ala	Val	Tyr	Tyr	Cys
			85						90					95	
Ala	Arg	Glu	Ser	Pro	Tyr	Phe	Ser	Asn	Leu	Tyr	Val	Met	Asp	Tyr	Trp
			100					105					110		
Gly	Gln	Gly	Thr	Ser	Val	Thr	Val	Ser	Ser						
		115					120								

```
<210> SEQ ID NO 10
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(111)
<223> OTHER INFORMATION: Fab 0301 light chain variable region
```

<400> SEQUENCE: 10

Asn	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Ser	Leu	Ala	Val	Ser	Leu	Gly
1				5					10					15	
Gln	Arg	Ala	Thr	Ile	Ser	Cys	Lys	Ala	Ser	Gln	Ser	Val	Asp	Tyr	Asp
			20					25					30		
Gly	Asp	Asn	Tyr	Met	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro
		35					40					45			
Lys	Leu	Leu	Ile	Tyr	Ala	Ala	Ser	Asn	Leu	Glu	Ser	Gly	Ile	Pro	Ala
	50					55					60				
Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Asn	Ile	His
65					70					75					80
Pro	Val	Glu	Glu	Glu	Asp	Ala	Ala	Thr	Tyr	Tyr	Cys	His	Leu	Ser	Asn
				85					90					95	
Glu	Asp	Leu	Ser	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys	
		100						105					110		

```
<210> SEQ ID NO 11
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(121)
<223> OTHER INFORMATION: Fab 0302 heavy chain variable region
```

<400> SEQUENCE: 11

Glu 1	Ile	Gln	Leu	Gln 5	Gln	Ser	Gly	Pro	Glu 10	Leu	Val	Lys	Pro	Gly 15	Ala
Ser	Val	Lys	Met 20	Ser	Cys	Lys	Ala	Ser 25	Gly	Tyr	Thr	Phe	Ser 30	Asp	Phe
Asn	Ile	His 35	Trp	Val	Lys	Gln	Lys 40	Pro	Gly	Gln	Gly	Leu 45	Glu	Trp	Ile
Gly	Tyr 50	Ile	Asn	Pro	Tyr	Thr 55	Asp	Val	Thr	Val	Tyr 60	Asn	Glu	Lys	Phe
Lys 65	Gly	Lys	Ala	Thr	Leu 70	Thr	Ser	Asp	Arg	Ser 75	Ser	Ser	Thr	Ala	Tyr 80
Met	Asp	Leu	Ser	Ser 85	Leu	Thr	Ser	Glu	Asp 90	Ser	Ala	Val	Tyr	Tyr 95	Cys
Ala	Ser	Tyr	Phe 100	Asp	Gly	Thr	Phe	Asp 105	Tyr	Ala	Leu	Asp 110	Tyr	Trp	Gly
Gln	Gly	Thr 115	Ser	Ile	Thr	Val	Ser	Ser 120							

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<210> SEQ ID NO 12
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(111)
<223> OTHER INFORMATION: Fab 0302 light chain variable region

```

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<400> SEQUENCE: 12

```

```

Asp Val Val Val Thr Gln Thr Pro Ala Ser Leu Ala Val Ser Leu Gly
 1              5              10              15

Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr
      20              25              30

Gly Leu Ser Phe Met Asn Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro
      35              40              45

Lys Leu Leu Ile Tyr Thr Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
      50              55              60

Arg Phe Ser Gly Gly Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asp
 65              70              75              80

Pro Val Glu Ala Asp Asp Ala Ala Thr Tyr Phe Cys Gln Gln Ser Lys
      85              90              95

Glu Leu Pro Trp Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile Lys
      100              105              110

```

```

<210> SEQ ID NO 13
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(122)
<223> OTHER INFORMATION: Fab 0311 heavy chain variable region

```

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<400> SEQUENCE: 13

```

```

Glu Ile Gln Leu Gln Gln Ser Gly Pro Asp Leu Met Lys Pro Gly Ala
 1              5              10              15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asp Tyr
      20              25              30

Asn Met His Trp Val Lys Gln Asn Gln Gly Lys Ser Leu Glu Trp Met
      35              40              45

Gly Glu Ile Asn Pro Asn Asn Gly Val Val Val Tyr Asn Gln Lys Phe
      50              55              60

Lys Gly Thr Thr Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
 65              70              75              80

Met Asp Leu His Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
      85              90              95

Thr Arg Ala Leu Tyr His Ser Asn Phe Gly Trp Tyr Phe Asp Ser Trp
      100              105              110

Gly Lys Gly Thr Thr Leu Thr Val Ser Ser
      115              120

```

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<210> SEQ ID NO 14
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(111)
<223> OTHER INFORMATION: Fab 0311 light chain variable region

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<400> SEQUENCE: 14

```

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1           5           10           15
Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20           25           30
Gly Asp Ser His Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35           40           45
Lys Leu Leu Ile Tyr Thr Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50           55           60
Arg Phe Ser Gly Ser Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile His
65           70           75           80
Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Gly Asn
85           90           95
Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile Lys
100          105          110

```

<210> SEQ ID NO 15

<211> LENGTH: 10

<212> TYPE: PRT

<213> ORGANISM: Mus musculus

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(10)

<223> OTHER INFORMATION: 0301 heavy chain CDR1

<400> SEQUENCE: 15

```

Gly Tyr Thr Phe Thr Asp Asn Tyr Met Ile
1           5           10

```

<210> SEQ ID NO 16

<211> LENGTH: 17

<212> TYPE: PRT

<213> ORGANISM: Mus musculus

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(17)

<223> OTHER INFORMATION: 0301 heavy chain CDR2

<400> SEQUENCE: 16

```

Asp Ile Asn Pro Tyr Asn Gly Gly Thr Thr Phe Asn Gln Lys Phe Lys
1           5           10           15

```

Gly

<210> SEQ ID NO 17

<211> LENGTH: 13

<212> TYPE: PRT

<213> ORGANISM: Mus musculus

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(13)

<223> OTHER INFORMATION: 0301 heavy chain CDR3

<400> SEQUENCE: 17

```

Glu Ser Pro Tyr Phe Ser Asn Leu Tyr Val Met Asp Tyr
1           5           10

```

<210> SEQ ID NO 18

<211> LENGTH: 15

<212> TYPE: PRT

<213> ORGANISM: Mus musculus

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(15)

<223> OTHER INFORMATION: 0301 light chain CDR1

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<400> SEQUENCE: 18

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Asn Tyr Met Asn
1 5 10 15

<210> SEQ ID NO 19

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Mus musculus

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(7)

<223> OTHER INFORMATION: 0301 light chain CDR2

<400> SEQUENCE: 19

Ala Ala Ser Asn Leu Glu Ser
1 5

<210> SEQ ID NO 20

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Mus musculus

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(9)

<223> OTHER INFORMATION: 0301 light chain CDR3

<400> SEQUENCE: 20

His Leu Ser Asn Glu Asp Leu Ser Thr
1 5

<210> SEQ ID NO 21

<211> LENGTH: 10

<212> TYPE: PRT

<213> ORGANISM: Mus musculus

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(10)

<223> OTHER INFORMATION: 0302 heavy chain CDR1

<400> SEQUENCE: 21

Gly Tyr Thr Phe Ser Asp Phe Asn Ile His
1 5 10

<210> SEQ ID NO 22

<211> LENGTH: 17

<212> TYPE: PRT

<213> ORGANISM: Mus musculus

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(17)

<223> OTHER INFORMATION: 0302 heavy chain CDR2

<400> SEQUENCE: 22

Tyr Ile Asn Pro Tyr Thr Asp Val Thr Val Tyr Asn Glu Lys Phe Lys
1 5 10 15

Gly

<210> SEQ ID NO 23

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Mus musculus

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(12)

<223> OTHER INFORMATION: 0302 heavy chain CDR3

<400> SEQUENCE: 23

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Tyr Phe Asp Gly Thr Phe Asp Tyr Ala Leu Asp Tyr
1 5 10

<210> SEQ ID NO 24
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: 0302 light chain CDR1

<400> SEQUENCE: 24

Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly Leu Ser Phe Met Asn
1 5 10 15

<210> SEQ ID NO 25
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(7)
<223> OTHER INFORMATION: 0302 light chain CDR2

<400> SEQUENCE: 25

Thr Ala Ser Asn Leu Glu Ser
1 5

<210> SEQ ID NO 26
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(9)
<223> OTHER INFORMATION: 0302 light chain CDR3

<400> SEQUENCE: 26

Gln Gln Ser Lys Glu Leu Pro Trp Thr
1 5

<210> SEQ ID NO 27
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(10)
<223> OTHER INFORMATION: 0311 heavy chain CDR1

<400> SEQUENCE: 27

Gly Tyr Ile Phe Thr Asp Tyr Asn Met His
1 5 10

<210> SEQ ID NO 28
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(17)
<223> OTHER INFORMATION: 0311 heavy chain CDR2

<400> SEQUENCE: 28

Glu Ile Asn Pro Asn Asn Gly Val Val Val Tyr Asn Gln Lys Phe Lys
1 5 10 15

-continued

Gly

<210> SEQ ID NO 29
 <211> LENGTH: 13
 <212> TYPE: PRT
 <213> ORGANISM: Mus musculus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(13)
 <223> OTHER INFORMATION: 0311 heavy chain CDR3

<400> SEQUENCE: 29

Ala Leu Tyr His Ser Asn Phe Gly Trp Tyr Phe Asp Ser
 1 5 10

<210> SEQ ID NO 30
 <211> LENGTH: 15
 <212> TYPE: PRT
 <213> ORGANISM: Mus musculus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(15)
 <223> OTHER INFORMATION: 0311 light chain CDR1

<400> SEQUENCE: 30

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser His Met Asn
 1 5 10 15

<210> SEQ ID NO 31
 <211> LENGTH: 7
 <212> TYPE: PRT
 <213> ORGANISM: Mus musculus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(7)
 <223> OTHER INFORMATION: 0311 light chain CDR2

<400> SEQUENCE: 31

Thr Ala Ser Asn Leu Glu Ser
 1 5

<210> SEQ ID NO 32
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Mus musculus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(9)
 <223> OTHER INFORMATION: 0311 light chain CDR3

<400> SEQUENCE: 32

Gln Gln Gly Asn Glu Asp Pro Trp Thr
 1 5

<210> SEQ ID NO 33
 <211> LENGTH: 449
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: cAb 0301 heavy chain

<400> SEQUENCE: 33

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Arg Pro Gly Ala
 1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Asn
 20 25 30

Tyr Met Ile Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile

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35					40					45					
Gly	Asp	Ile	Asn	Pro	Tyr	Asn	Gly	Gly	Thr	Thr	Phe	Asn	Gln	Lys	Phe
50						55					60				
Lys	Gly	Lys	Ala	Thr	Leu	Thr	Val	Glu	Lys	Ser	Ser	Ser	Thr	Ala	Tyr
65					70					75					80
Met	Gln	Leu	Asn	Ser	Leu	Thr	Ser	Glu	Asp	Ser	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Ala	Arg	Glu	Ser	Pro	Tyr	Phe	Ser	Asn	Leu	Tyr	Val	Met	Asp	Tyr	Trp
				100					105				110		
Gly	Gln	Gly	Thr	Ser	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro
													125		
Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser	Thr
						135					140				
Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr
145					150					155					160
Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro
				165					170					175	
Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr
				180					185				190		
Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Lys	Thr	Tyr	Thr	Cys	Asn	Val	Asp
				195					200				205		
His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Ser	Lys	Tyr
	210					215					220				
Gly	Pro	Pro	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Phe	Leu	Gly	Gly	Pro
225					230					235					240
Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser
				245					250					255	
Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	Gln	Glu	Asp
				260					265				270		
Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn
				275					280				285		
Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Tyr	Arg	Val
	290					295					300				
Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu
305					310					315					320
Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ser	Ser	Ile	Glu	Lys
				325					330					335	
Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr
				340					345				350		
Leu	Pro	Pro	Ser	Gln	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr
				355					360				365		
Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu
	370					375					380				
Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu
385					390					395					400
Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys
				405					410					415	
Ser	Arg	Trp	Gln	Glu	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu
				420					425				430		
Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly
				435					440				445		

Lys

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<210> SEQ ID NO 34
 <211> LENGTH: 218
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: cAb 0301 light chain

<400> SEQUENCE: 34

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Asn Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1             5             10             15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
                20             25             30

Gly Asp Asn Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
            35             40             45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
            50             55             60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65             70             75             80

Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys His Leu Ser Asn
            85             90             95

Glu Asp Leu Ser Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
            100            105            110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
            115            120            125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
            130            135            140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145            150            155            160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
            165            170            175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180            185            190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
            195            200            205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210            215
  
```

<210> SEQ ID NO 35
 <211> LENGTH: 448
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: cAb 0302 heavy chain

<400> SEQUENCE: 35

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Glu Ile Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1             5             10             15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asp Phe
            20             25             30

Asn Ile His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
            35             40             45

Gly Tyr Ile Asn Pro Tyr Thr Asp Val Thr Val Tyr Asn Glu Lys Phe
            50             55             60

Lys Gly Lys Ala Thr Leu Thr Ser Asp Arg Ser Ser Ser Thr Ala Tyr
65             70             75             80

Met Asp Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
            85             90             95
  
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Ala Ser Tyr Phe Asp Gly Thr Phe Asp Tyr Ala Leu Asp Tyr Trp Gly
 100 105 110
 Gln Gly Thr Ser Ile Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125
 Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
 130 135 140
 Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160
 Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175
 Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190
 Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
 195 200 205
 Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
 210 215 220
 Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
 225 230 235 240
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 245 250 255
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
 260 265 270
 Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 275 280 285
 Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
 290 295 300
 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 305 310 315 320
 Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
 325 330 335
 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 340 345 350
 Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 355 360 365
 Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 370 375 380
 Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 385 390 395 400
 Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
 405 410 415
 Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 420 425 430
 Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
 435 440 445

<210> SEQ ID NO 36

<211> LENGTH: 218

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic: cAb 0302 light chain

<400> SEQUENCE: 36

Asp Val Val Val Thr Gln Thr Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

-continued

Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr
 20 25 30
 Gly Leu Ser Phe Met Asn Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45
 Lys Leu Leu Ile Tyr Thr Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
 50 55 60
 Arg Phe Ser Gly Gly Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asp
 65 70 75 80
 Pro Val Glu Ala Asp Asp Ala Ala Thr Tyr Phe Cys Gln Gln Ser Lys
 85 90 95
 Glu Leu Pro Trp Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile Lys Arg
 100 105 110
 Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
 115 120 125
 Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
 130 135 140
 Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
 145 150 155 160
 Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
 165 170 175
 Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
 180 185 190
 His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
 195 200 205
 Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 210 215

<210> SEQ ID NO 37
 <211> LENGTH: 449
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: cAb 0311 heavy chain

<400> SEQUENCE: 37

Glu Ile Gln Leu Gln Gln Ser Gly Pro Asp Leu Met Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asp Tyr
 20 25 30
 Asn Met His Trp Val Lys Gln Asn Gln Gly Lys Ser Leu Glu Trp Met
 35 40 45
 Gly Glu Ile Asn Pro Asn Asn Gly Val Val Val Tyr Asn Gln Lys Phe
 50 55 60
 Lys Gly Thr Thr Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80
 Met Asp Leu His Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
 85 90 95
 Thr Arg Ala Leu Tyr His Ser Asn Phe Gly Trp Tyr Phe Asp Ser Trp
 100 105 110
 Gly Lys Gly Thr Thr Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
 115 120 125
 Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
 130 135 140
 Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
 145 150 155 160

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Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro
			165						170					175	
Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr
		180						185					190		
Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Lys	Thr	Tyr	Thr	Cys	Asn	Val	Asp
		195					200					205			
His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Ser	Lys	Tyr
	210					215					220				
Gly	Pro	Pro	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Phe	Leu	Gly	Gly	Pro
225				230						235					240
Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser
			245						250					255	
Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	Gln	Glu	Asp
			260					265					270		
Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn
		275					280					285			
Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Tyr	Arg	Val
	290					295					300				
Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu
305					310					315					320
Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ser	Ser	Ile	Glu	Lys
			325						330					335	
Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr
			340					345					350		
Leu	Pro	Pro	Ser	Gln	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr
		355					360					365			
Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu
	370					375				380					
Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu
385				390						395					400
Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys
			405						410					415	
Ser	Arg	Trp	Gln	Glu	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu
			420					425					430		
Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly
		435					440					445			

Lys

<210> SEQ ID NO 38
 <211> LENGTH: 218
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: cAb 0311 light chain

<400> SEQUENCE: 38

Asp	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Ser	Leu	Ala	Val	Ser	Leu	Gly
1				5					10					15	
Gln	Arg	Ala	Thr	Ile	Ser	Cys	Lys	Ala	Ser	Gln	Ser	Val	Asp	Tyr	Asp
		20						25					30		
Gly	Asp	Ser	His	Met	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro
	35					40						45			
Lys	Leu	Leu	Ile	Tyr	Thr	Ala	Ser	Asn	Leu	Glu	Ser	Gly	Ile	Pro	Ala
	50					55						60			

-continued

Arg Phe Ser Gly Ser Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile His
 65 70 75 80
 Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Gly Asn
 85 90 95
 Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile Lys Arg
 100 105 110
 Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
 115 120 125
 Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
 130 135 140
 Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
 145 150 155 160
 Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
 165 170 175
 Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
 180 185 190
 His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
 195 200 205
 Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 210 215

<210> SEQ ID NO 39
 <211> LENGTH: 122
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: h0301-H0 heavy chain variable region

<400> SEQUENCE: 39

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Asn
 20 25 30
 Tyr Met Ile Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Asp Ile Asn Pro Tyr Asn Gly Gly Thr Thr Phe Asn Gln Lys Phe
 50 55 60
 Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Glu Ser Pro Tyr Phe Ser Asn Leu Tyr Val Met Asp Tyr Trp
 100 105 110
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 40
 <211> LENGTH: 122
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: h0301-H1 heavy chain variable region

<400> SEQUENCE: 40

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Asn
 20 25 30

-continued

Tyr Met Ile Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Asp Ile Asn Pro Tyr Asn Gly Gly Thr Thr Phe Asn Gln Lys Phe
 50 55 60
 Lys Gly Arg Val Thr Ile Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Glu Ser Pro Tyr Phe Ser Asn Leu Tyr Val Met Asp Tyr Trp
 100 105 110
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 41
 <211> LENGTH: 122
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: h0301-H2 heavy chain variable region

<400> SEQUENCE: 41

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Asn
 20 25 30
 Tyr Met Ile Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Asp Ile Asn Pro Tyr Asn Gly Gly Thr Thr Phe Asn Gln Lys Phe
 50 55 60
 Lys Gly Arg Ala Thr Leu Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Glu Ser Pro Tyr Phe Ser Asn Leu Tyr Val Met Asp Tyr Trp
 100 105 110
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 42
 <211> LENGTH: 121
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0302-H1 heavy chain variable region

<400> SEQUENCE: 42

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asp Phe
 20 25 30
 Asn Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Tyr Ile Asn Pro Tyr Thr Asp Val Thr Val Tyr Asn Glu Lys Phe
 50 55 60
 Lys Gly Arg Val Thr Ile Thr Ser Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

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85	90	95
Ala Ser Tyr Phe Asp Gly Thr Phe Asp Tyr Ala Leu Asp Tyr Trp Gly		
100	105	110
Gln Gly Thr Leu Val Thr Val Ser Ser		
115	120	

<210> SEQ ID NO 43
 <211> LENGTH: 121
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0302-H2 heavy chain variable region

<400> SEQUENCE: 43

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser		
1	5	10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asp Phe		
20	25	30
Asn Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile		
35	40	45
Gly Tyr Ile Asn Pro Tyr Thr Asp Val Thr Val Tyr Asn Glu Lys Phe		
50	55	60
Lys Gly Arg Ala Thr Leu Thr Ser Asp Lys Ser Thr Ser Thr Ala Tyr		
65	70	75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys		
85	90	95
Ala Ser Tyr Phe Asp Gly Thr Phe Asp Tyr Ala Leu Asp Tyr Trp Gly		
100	105	110
Gln Gly Thr Leu Val Thr Val Ser Ser		
115	120	

<210> SEQ ID NO 44
 <211> LENGTH: 122
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0311-H1 heavy chain variable region

<400> SEQUENCE: 44

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser		
1	5	10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asp Tyr		
20	25	30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met		
35	40	45
Gly Glu Ile Asn Pro Asn Asn Gly Val Val Val Tyr Asn Gln Lys Phe		
50	55	60
Lys Gly Arg Val Thr Ile Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr		
65	70	75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys		
85	90	95
Thr Arg Ala Leu Tyr His Ser Asn Phe Gly Trp Tyr Phe Asp Ser Trp		
100	105	110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser		
115	120	

<210> SEQ ID NO 45
 <211> LENGTH: 122

-continued

<212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0311-H2 heavy chain variable region

<400> SEQUENCE: 45

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asp Tyr
 20 25 30
 Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Glu Ile Asn Pro Asn Asn Gly Val Val Val Tyr Asn Gln Lys Phe
 50 55 60
 Lys Gly Thr Thr Thr Leu Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Thr Arg Ala Leu Tyr His Ser Asn Phe Gly Trp Tyr Phe Asp Ser Trp
 100 105 110
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 46
 <211> LENGTH: 111
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: h0301-L0 light chain variable region

<400> SEQUENCE: 46

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30
 Gly Asp Asn Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
 35 40 45
 Arg Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
 65 70 75 80
 Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys His Leu Ser Asn
 85 90 95
 Glu Asp Leu Ser Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> SEQ ID NO 47
 <211> LENGTH: 111
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: h0301-L1 light chain variable region

<400> SEQUENCE: 47

Asn Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30
 Gly Asp Asn Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro

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35	40	45
Arg Leu Leu Ile Tyr Ala	Ala Ser Asn Leu Glu	Ser Gly Ile Pro Ala
50	55	60
Arg Phe Ser Gly Ser Gly	Ser Gly Thr Asp Phe	Thr Leu Thr Ile Ser
65	70	75 80
Ser Leu Glu Pro Glu Asp	Phe Ala Val Tyr Tyr	Cys His Leu Ser Asn
85	90	95
Glu Asp Leu Ser Thr Phe	Gly Gly Gly Thr Lys	Val Glu Ile Lys
100	105	110

<210> SEQ ID NO 48
 <211> LENGTH: 111
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0302-L0 light chain variable region

<400> SEQUENCE: 48

Glu Ile Val Leu Thr Gln	Ser Pro Ala Thr Leu	Ser Leu Ser Pro Gly
1	5 10	15
Glu Arg Ala Thr Leu Ser	Cys Arg Ala Ser Glu	Ser Val Asp Asn Tyr
20	25	30
Gly Leu Ser Phe Met Asn	Trp Tyr Gln Gln Lys	Pro Gly Gln Ala Pro
35	40	45
Arg Leu Leu Ile Tyr Thr	Ala Ser Asn Leu Glu	Ser Gly Ile Pro Ala
50	55	60
Arg Phe Ser Gly Ser Gly	Ser Gly Thr Asp Phe	Thr Leu Thr Ile Ser
65	70	75 80
Ser Leu Glu Pro Glu Asp	Phe Ala Val Tyr Tyr	Cys Gln Gln Ser Lys
85	90	95
Glu Leu Pro Trp Thr Phe	Gly Gln Gly Thr Lys	Val Glu Ile Lys
100	105	110

<210> SEQ ID NO 49
 <211> LENGTH: 111
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0302-L1 light chain variable region

<400> SEQUENCE: 49

Glu Ile Val Leu Thr Gln	Ser Pro Ala Thr Leu	Ser Leu Ser Pro Gly
1	5 10	15
Glu Arg Ala Thr Leu Ser	Cys Arg Ala Ser Glu	Ser Val Asp Asn Tyr
20	25	30
Gly Leu Ser Phe Met Asn	Trp Tyr Gln Gln Lys	Pro Gly Gln Ala Pro
35	40	45
Arg Leu Leu Ile Tyr Thr	Ala Ser Asn Leu Glu	Ser Gly Ile Pro Ala
50	55	60
Arg Phe Ser Gly Ser Gly	Ser Arg Thr Asp Phe	Thr Leu Thr Ile Ser
65	70	75 80
Ser Leu Glu Pro Glu Asp	Phe Ala Val Tyr Tyr	Cys Gln Gln Ser Lys
85	90	95
Glu Leu Pro Trp Thr Phe	Gly Gln Gly Thr Lys	Val Glu Ile Lys
100	105	110

<210> SEQ ID NO 50
 <211> LENGTH: 111

-continued

<212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0302-L2 light chain variable region

<400> SEQUENCE: 50

Glu Ile Val Val Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr
 20 25 30
 Gly Leu Ser Phe Met Asn Trp Phe Gln Gln Lys Pro Gly Gln Ala Pro
 35 40 45
 Arg Leu Leu Ile Tyr Thr Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser
 65 70 75 80
 Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Lys
 85 90 95
 Glu Leu Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> SEQ ID NO 51
 <211> LENGTH: 111
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0311-L0 light chain variable region

<400> SEQUENCE: 51

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30
 Gly Asp Ser His Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
 35 40 45
 Arg Leu Leu Ile Tyr Thr Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
 65 70 75 80
 Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Gly Asn
 85 90 95
 Glu Asp Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> SEQ ID NO 52
 <211> LENGTH: 111
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0311-L1 light chain variable region

<400> SEQUENCE: 52

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30
 Gly Asp Ser His Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
 35 40 45
 Arg Leu Leu Ile Tyr Thr Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala

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50	55	60
Arg Phe Ser Gly Ser Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile Ser		
65	70	75 80
Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Gly Asn		
	85	90 95
Glu Asp Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys		
	100	105 110

<210> SEQ ID NO 53
 <211> LENGTH: 449
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: h0301-H0 heavy chain

<400> SEQUENCE: 53

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser	
1	5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Asn	
	20 25 30
Tyr Met Ile Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met	
	35 40 45
Gly Asp Ile Asn Pro Tyr Asn Gly Gly Thr Thr Phe Asn Gln Lys Phe	
	50 55 60
Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr	
	65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys	
	85 90 95
Ala Arg Glu Ser Pro Tyr Phe Ser Asn Leu Tyr Val Met Asp Tyr Trp	
	100 105 110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro	
	115 120 125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr	
	130 135 140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr	
	145 150 155 160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro	
	165 170 175
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr	
	180 185 190
Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp	
	195 200 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr	
	210 215 220
Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro	
	225 230 235 240
Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser	
	245 250 255
Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp	
	260 265 270
Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn	
	275 280 285
Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val	
	290 295 300
Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu	

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305	310	315	320
Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys	325	330	335
Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr	340	345	350
Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr	355	360	365
Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu	370	375	380
Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu	385	390	400
Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys	405	410	415
Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu	420	425	430
Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly	435	440	445

Lys

<210> SEQ ID NO 54

<211> LENGTH: 449

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic: h0301-H1 heavy chain

<400> SEQUENCE: 54

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser	1	5	10	15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Asn	20	25	30	
Tyr Met Ile Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met	35	40	45	
Gly Asp Ile Asn Pro Tyr Asn Gly Gly Thr Thr Phe Asn Gln Lys Phe	50	55	60	
Lys Gly Arg Val Thr Ile Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr	65	70	75	80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys	85	90	95	
Ala Arg Glu Ser Pro Tyr Phe Ser Asn Leu Tyr Val Met Asp Tyr Trp	100	105	110	
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro	115	120	125	
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr	130	135	140	
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr	145	150	155	160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro	165	170	175	
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr	180	185	190	
Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp	195	200	205	
His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr	210	215	220	

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Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro
 225 230 235 240
 Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
 245 250 255
 Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp
 260 265 270
 Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
 275 280 285
 Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val
 290 295 300
 Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 305 310 315 320
 Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
 325 330 335
 Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350
 Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365
 Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380
 Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400
 Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys
 405 410 415
 Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430
 Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
 435 440 445

Lys

<210> SEQ ID NO 55
 <211> LENGTH: 449
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: h0301-H2 heavy chain

<400> SEQUENCE: 55

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Asn
 20 25 30
 Tyr Met Ile Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Asp Ile Asn Pro Tyr Asn Gly Gly Thr Thr Phe Asn Gln Lys Phe
 50 55 60
 Lys Gly Arg Ala Thr Leu Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Glu Ser Pro Tyr Phe Ser Asn Leu Tyr Val Met Asp Tyr Trp
 100 105 110
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
 115 120 125

Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser	Thr
130						135					140				
Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr
145					150					155					160
Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro
			165						170					175	
Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr
		180						185					190		
Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Lys	Thr	Tyr	Thr	Cys	Asn	Val	Asp
	195					200						205			
His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Ser	Lys	Tyr
210						215					220				
Gly	Pro	Pro	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Phe	Leu	Gly	Gly	Pro
225					230					235					240
Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser
			245						250					255	
Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	Gln	Glu	Asp
		260						265					270		
Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn
	275					280						285			
Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Tyr	Arg	Val
290						295					300				
Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu
305					310					315					320
Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ser	Ser	Ile	Glu	Lys
		325						330					335		
Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr
		340						345				350			
Leu	Pro	Pro	Ser	Gln	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr
	355					360						365			
Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu
370					375					380					
Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu
385					390					395					400
Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys
		405							410					415	
Ser	Arg	Trp	Gln	Glu	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu
		420						425				430			
Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly
	435						440					445			

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asp Phe
20 25 30

Asn Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

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35					40					45					
Gly	Tyr	Ile	Asn	Pro	Tyr	Thr	Asp	Val	Thr	Val	Tyr	Asn	Glu	Lys	Phe
50					55					60					
Lys	Gly	Arg	Val	Thr	Ile	Thr	Ser	Asp	Lys	Ser	Thr	Ser	Thr	Ala	Tyr
65					70				75						80
Met	Glu	Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
			85						90					95	
Ala	Ser	Tyr	Phe	Asp	Gly	Thr	Phe	Asp	Tyr	Ala	Leu	Asp	Tyr	Trp	Gly
			100					105					110		
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser
			115					120					125		
Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser	Thr	Ala
			130			135						140			
Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val
145					150					155					160
Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala
			165						170					175	
Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val
			180						185				190		
Pro	Ser	Ser	Ser	Leu	Gly	Thr	Lys	Thr	Tyr	Thr	Cys	Asn	Val	Asp	His
			195					200					205		
Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Ser	Lys	Tyr	Gly
	210					215					220				
Pro	Pro	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Phe	Leu	Gly	Gly	Pro	Ser
225					230					235					240
Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg
			245						250					255	
Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	Gln	Glu	Asp	Pro
			260						265					270	
Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala
		275					280						285		
Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Tyr	Arg	Val	Val
	290					295						300			
Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr
305					310					315					320
Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ser	Ser	Ile	Glu	Lys	Thr
			325						330					335	
Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu
			340					345						350	
Pro	Pro	Ser	Gln	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys
		355					360						365		
Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser
	370					375					380				
Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp
385					390					395					400
Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys	Ser
			405						410					415	
Arg	Trp	Gln	Glu	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala
			420					425					430		
Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly	Lys
		435					440						445		

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<211> LENGTH: 448
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: H0302-H2 heavy chain

<400> SEQUENCE: 57

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1          5          10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asp Phe
20          25          30
Asn Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35          40          45
Gly Tyr Ile Asn Pro Tyr Thr Asp Val Thr Val Tyr Asn Glu Lys Phe
50          55          60
Lys Gly Arg Ala Thr Leu Thr Ser Asp Lys Ser Thr Ser Thr Ala Tyr
65          70          75          80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95
Ala Ser Tyr Phe Asp Gly Thr Phe Asp Tyr Ala Leu Asp Tyr Trp Gly
100         105         110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115         120         125
Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
130         135         140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145         150         155         160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165         170         175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180         185         190
Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His
195         200         205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly
210         215         220
Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
225         230         235         240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
245         250         255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
260         265         270
Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
275         280         285
Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
290         295         300
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305         310         315         320
Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
325         330         335
Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
340         345         350
Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
355         360         365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370         375         380

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Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 385 390 395 400
 Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
 405 410 415
 Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 420 425 430
 Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
 435 440 445

 <210> SEQ ID NO 58
 <211> LENGTH: 449
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0311-H1 heavy chain

 <400> SEQUENCE: 58

 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asp Tyr
 20 25 30
 Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Glu Ile Asn Pro Asn Asn Gly Val Val Val Tyr Asn Gln Lys Phe
 50 55 60
 Lys Gly Arg Val Thr Ile Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Thr Arg Ala Leu Tyr His Ser Asn Phe Gly Trp Tyr Phe Asp Ser Trp
 100 105 110
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
 115 120 125
 Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
 130 135 140
 Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
 145 150 155 160
 Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
 165 170 175
 Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
 180 185 190
 Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
 195 200 205
 His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
 210 215 220
 Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro
 225 230 235 240
 Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
 245 250 255
 Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp
 260 265 270
 Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
 275 280 285
 Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val
 290 295 300

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Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350

Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
 435 440 445

Lys

<210> SEQ ID NO 59
 <211> LENGTH: 449
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0311-H2 heavy chain

<400> SEQUENCE: 59

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asp Tyr
 20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Glu Ile Asn Pro Asn Asn Gly Val Val Val Tyr Asn Gln Lys Phe
 50 55 60

Lys Gly Thr Thr Thr Leu Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Thr Arg Ala Leu Tyr His Ser Asn Phe Gly Trp Tyr Phe Asp Ser Trp
 100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
 115 120 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
 130 135 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
 145 150 155 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
 165 170 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
 180 185 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
 195 200 205

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His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Ser	Lys	Tyr
210						215					220				
Gly	Pro	Pro	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Phe	Leu	Gly	Gly	Pro
225					230					235					240
Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser
				245						250				255	
Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	Gln	Glu	Asp
			260							265				270	
Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn
			275				280					285			
Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Tyr	Arg	Val
			290			295					300				
Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu
305					310					315					320
Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ser	Ser	Ile	Glu	Lys
				325					330					335	
Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr
			340					345					350		
Leu	Pro	Pro	Ser	Gln	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr
		355					360					365			
Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu
		370				375					380				
Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu
385					390					395					400
Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Arg	Leu	Thr	Val	Asp	Lys
			405						410					415	
Ser	Arg	Trp	Gln	Glu	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu
			420					425					430		
Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Leu	Gly
		435					440					445			

Lys

<210> SEQ ID NO 60
 <211> LENGTH: 218
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: h0301-L0 light chain

<400> SEQUENCE: 60

Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1				5					10					15	
Glu	Arg	Ala	Thr	Leu	Ser	Cys	Lys	Ala	Ser	Gln	Ser	Val	Asp	Tyr	Asp
		20						25					30		
Gly	Asp	Asn	Tyr	Met	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro
		35				40						45			
Arg	Leu	Leu	Ile	Tyr	Ala	Ala	Ser	Asn	Leu	Glu	Ser	Gly	Ile	Pro	Ala
	50					55						60			
Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser
65				70					75					80	
Ser	Leu	Glu	Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	His	Leu	Ser	Asn
			85					90					95		
Glu	Asp	Leu	Ser	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg
		100						105					110		
Thr	Val	Ala	Ala	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln

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115	120	125
Leu Lys Ser Gly Thr Ala	Ser Val Val Cys Leu	Leu Asn Asn Phe Tyr
130	135	140
Pro Arg Glu Ala Lys Val	Gln Trp Lys Val Asp	Asn Ala Leu Gln Ser
145	150	155
Gly Asn Ser Gln Glu Ser	Val Thr Glu Gln Asp	Ser Lys Asp Ser Thr
	165	170
Tyr Ser Leu Ser Ser Thr	Leu Thr Leu Ser Lys	Ala Asp Tyr Glu Lys
	180	185
His Lys Val Tyr Ala Cys	Glu Val Thr His Gln	Gly Leu Ser Ser Pro
	195	200
Val Thr Lys Ser Phe Asn	Arg Gly Glu Cys	
	210	215

<210> SEQ ID NO 61
 <211> LENGTH: 218
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: h0301-L1 light chain

<400> SEQUENCE: 61

Asn Ile Val Leu Thr Gln	Ser Pro Ala Thr Leu	Ser Leu Ser Pro Gly
1	5	10
Glu Arg Ala Thr Leu Ser	Cys Lys Ala Ser Gln	Ser Val Asp Tyr Asp
	20	25
Gly Asp Asn Tyr Met Asn	Trp Tyr Gln Gln Lys	Pro Gly Gln Ala Pro
	35	40
Arg Leu Leu Ile Tyr Ala	Ala Ser Asn Leu Glu	Ser Gly Ile Pro Ala
	50	55
Arg Phe Ser Gly Ser Gly	Ser Gly Thr Asp Phe	Thr Leu Thr Ile Ser
	65	70
Ser Leu Glu Pro Glu Asp	Phe Ala Val Tyr Tyr	Cys His Leu Ser Asn
	85	90
Glu Asp Leu Ser Thr Phe	Gly Gly Gly Thr Lys	Val Glu Ile Lys Arg
	100	105
Thr Val Ala Ala Pro Ser	Val Phe Ile Phe Pro	Pro Ser Asp Glu Gln
	115	120
Leu Lys Ser Gly Thr Ala	Ser Val Val Cys Leu	Leu Asn Asn Phe Tyr
	130	135
Pro Arg Glu Ala Lys Val	Gln Trp Lys Val Asp	Asn Ala Leu Gln Ser
	145	150
Gly Asn Ser Gln Glu Ser	Val Thr Glu Gln Asp	Ser Lys Asp Ser Thr
	165	170
Tyr Ser Leu Ser Ser Thr	Leu Thr Leu Ser Lys	Ala Asp Tyr Glu Lys
	180	185
His Lys Val Tyr Ala Cys	Glu Val Thr His Gln	Gly Leu Ser Ser Pro
	195	200
Val Thr Lys Ser Phe Asn	Arg Gly Glu Cys	
	210	215

<210> SEQ ID NO 62
 <211> LENGTH: 218
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0302-L0 light chain

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<400> SEQUENCE: 62

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr
 20 25 30
 Gly Leu Ser Phe Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
 35 40 45
 Arg Leu Leu Ile Tyr Thr Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
 65 70 75 80
 Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Lys
 85 90 95
 Glu Leu Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
 100 105 110
 Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
 115 120 125
 Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
 130 135 140
 Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
 145 150 155 160
 Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
 165 170 175
 Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
 180 185 190
 His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
 195 200 205
 Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 210 215

<210> SEQ ID NO 63

<211> LENGTH: 218

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic: H0302-L1 light chain

<400> SEQUENCE: 63

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr
 20 25 30
 Gly Leu Ser Phe Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
 35 40 45
 Arg Leu Leu Ile Tyr Thr Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser
 65 70 75 80
 Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Lys
 85 90 95
 Glu Leu Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
 100 105 110
 Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
 115 120 125

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Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
 130                      135                      140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                      150                      155                      160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                      165                      170                      175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
                      180                      185                      190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
                      195                      200                      205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 210                      215

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<210> SEQ ID NO 64
<211> LENGTH: 218
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: H0302-L2 light chain

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<400> SEQUENCE: 64

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Glu Ile Val Val Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1                      5                      10                      15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr
                      20                      25                      30

Gly Leu Ser Phe Met Asn Trp Phe Gln Gln Lys Pro Gly Gln Ala Pro
                      35                      40                      45

Arg Leu Leu Ile Tyr Thr Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
                      50                      55                      60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser
65                      70                      75                      80

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Lys
                      85                      90                      95

Glu Leu Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
                      100                      105                      110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
                      115                      120                      125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130                      135                      140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                      150                      155                      160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                      165                      170                      175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
                      180                      185                      190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195                      200                      205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 210                      215

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<210> SEQ ID NO 65
<211> LENGTH: 218
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: H0311-L0 light chain

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<400> SEQUENCE: 65

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Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30
 Gly Asp Ser His Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
 35 40 45
 Arg Leu Leu Ile Tyr Thr Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
 65 70 75 80
 Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Gly Asn
 85 90 95
 Glu Asp Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
 100 105 110
 Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
 115 120 125
 Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
 130 135 140
 Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
 145 150 155 160
 Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
 165 170 175
 Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
 180 185 190
 His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
 195 200 205
 Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 210 215

<210> SEQ ID NO 66
 <211> LENGTH: 218
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: H0311-L1 light chain

<400> SEQUENCE: 66

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
 20 25 30
 Gly Asp Ser His Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
 35 40 45
 Arg Leu Leu Ile Tyr Thr Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile Ser
 65 70 75 80
 Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Gly Asn
 85 90 95
 Glu Asp Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
 100 105 110
 Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
 115 120 125
 Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
 130 135 140

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Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
 145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
 165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
 180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
 195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 210 215

<210> SEQ ID NO 67
 <211> LENGTH: 158
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(158)
 <223> OTHER INFORMATION: Human CSF1

<400> SEQUENCE: 67

Glu Glu Val Ser Glu Tyr Cys Ser His Met Ile Gly Ser Gly His Leu
 1 5 10 15

Gln Ser Leu Gln Arg Leu Ile Asp Ser Gln Met Glu Thr Ser Cys Gln
 20 25 30

Ile Thr Phe Glu Phe Val Asp Gln Glu Gln Leu Lys Asp Pro Val Cys
 35 40 45

Tyr Leu Lys Lys Ala Phe Leu Leu Val Gln Asp Ile Met Glu Asp Thr
 50 55 60

Met Arg Phe Arg Asp Asn Thr Pro Asn Ala Ile Ala Ile Val Gln Leu
 65 70 75 80

Gln Glu Leu Ser Leu Arg Leu Lys Ser Cys Phe Thr Lys Asp Tyr Glu
 85 90 95

Glu His Asp Lys Ala Cys Val Arg Thr Phe Tyr Glu Thr Pro Leu Gln
 100 105 110

Leu Leu Glu Lys Val Lys Asn Val Phe Asn Glu Thr Lys Asn Leu Leu
 115 120 125

Asp Lys Asp Trp Asn Ile Phe Ser Lys Asn Cys Asn Asn Ser Phe Ala
 130 135 140

Glu Cys Ser Ser Gln Gly His Glu Arg Gln Ser Glu Gly Ser
 145 150 155

<210> SEQ ID NO 68
 <211> LENGTH: 222
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(222)
 <223> OTHER INFORMATION: Human IL34

<400> SEQUENCE: 68

Asn Glu Pro Leu Glu Met Trp Pro Leu Thr Gln Asn Glu Glu Cys Thr
 1 5 10 15

Val Thr Gly Phe Leu Arg Asp Lys Leu Gln Tyr Arg Ser Arg Leu Gln
 20 25 30

Tyr Met Lys His Tyr Phe Pro Ile Asn Tyr Lys Ile Ser Val Pro Tyr
 35 40 45

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Glu Gly Val Phe Arg Ile Ala Asn Val Thr Arg Leu Gln Arg Ala Gln
 50 55 60
 Val Ser Glu Arg Glu Leu Arg Tyr Leu Trp Val Leu Val Ser Leu Ser
 65 70 75 80
 Ala Thr Glu Ser Val Gln Asp Val Leu Leu Glu Gly His Pro Ser Trp
 85 90 95
 Lys Tyr Leu Gln Glu Val Gln Thr Leu Leu Leu Asn Val Gln Gln Gly
 100 105 110
 Leu Thr Asp Val Glu Val Ser Pro Lys Val Glu Ser Val Leu Ser Leu
 115 120 125
 Leu Asn Ala Pro Gly Pro Asn Leu Lys Leu Val Arg Pro Lys Ala Leu
 130 135 140
 Leu Asp Asn Cys Phe Arg Val Met Glu Leu Leu Tyr Cys Ser Cys Cys
 145 150 155 160
 Lys Gln Ser Ser Val Leu Asn Trp Gln Asp Cys Glu Val Pro Ser Pro
 165 170 175
 Gln Ser Cys Ser Pro Glu Pro Ser Leu Gln Tyr Ala Ala Thr Gln Leu
 180 185 190
 Tyr Pro Pro Pro Pro Trp Ser Pro Ser Ser Pro Pro His Ser Thr Gly
 195 200 205
 Ser Val Arg Pro Val Arg Ala Gln Gly Glu Gly Leu Leu Pro
 210 215 220

<210> SEQ ID NO 69
 <211> LENGTH: 25
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(25)
 <223> OTHER INFORMATION: Human acceptor A FR1

<400> SEQUENCE: 69

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser
 20 25

<210> SEQ ID NO 70
 <211> LENGTH: 14
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(14)
 <223> OTHER INFORMATION: Human acceptor A FR2

<400> SEQUENCE: 70

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
 1 5 10

<210> SEQ ID NO 71
 <211> LENGTH: 32
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(32)
 <223> OTHER INFORMATION: Human acceptor A FR3

<400> SEQUENCE: 71

Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu

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1	5	10	15
Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg			
	20	25	30

<210> SEQ ID NO 72
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(11)
 <223> OTHER INFORMATION: Human acceptor A FR4

<400> SEQUENCE: 72

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 73
 <211> LENGTH: 25
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(25)
 <223> OTHER INFORMATION: Human acceptor B FR1

<400> SEQUENCE: 73

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
20 25

<210> SEQ ID NO 74
 <211> LENGTH: 14
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(14)
 <223> OTHER INFORMATION: Human acceptor B FR2

<400> SEQUENCE: 74

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
1 5 10

<210> SEQ ID NO 75
 <211> LENGTH: 32
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(32)
 <223> OTHER INFORMATION: Human acceptor B FR3

<400> SEQUENCE: 75

Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

<210> SEQ ID NO 76
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(11)

-continued

<223> OTHER INFORMATION: Human acceptor B FR4

<400> SEQUENCE: 76

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 1 5 10

<210> SEQ ID NO 77

<211> LENGTH: 25

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(25)

<223> OTHER INFORMATION: Human acceptor C FR1

<400> SEQUENCE: 77

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser
 20 25

<210> SEQ ID NO 78

<211> LENGTH: 14

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(14)

<223> OTHER INFORMATION: Human acceptor C FR2

<400> SEQUENCE: 78

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
 1 5 10

<210> SEQ ID NO 79

<211> LENGTH: 32

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(32)

<223> OTHER INFORMATION: Human acceptor C FR3

<400> SEQUENCE: 79

Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
 1 5 10 15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
 20 25 30

<210> SEQ ID NO 80

<211> LENGTH: 11

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (1)..(11)

<223> OTHER INFORMATION: Human acceptor C FR4

<400> SEQUENCE: 80

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 1 5 10

<210> SEQ ID NO 81

<211> LENGTH: 23

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<220> FEATURE:

-continued

<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(23)
<223> OTHER INFORMATION: Human acceptor D FR1

<400> SEQUENCE: 81

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys
20

<210> SEQ ID NO 82
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: Human acceptor D FR2

<400> SEQUENCE: 82

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 83
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(32)
<223> OTHER INFORMATION: Human acceptor D FR3

<400> SEQUENCE: 83

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 84
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(10)
<223> OTHER INFORMATION: Human acceptor D FR4

<400> SEQUENCE: 84

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
1 5 10

<210> SEQ ID NO 85
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(23)
<223> OTHER INFORMATION: Human acceptor E FR1

<400> SEQUENCE: 85

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys
20

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<210> SEQ ID NO 86
 <211> LENGTH: 15
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(15)
 <223> OTHER INFORMATION: Human acceptor E FR2

<400> SEQUENCE: 86

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
 1 5 10 15

<210> SEQ ID NO 87
 <211> LENGTH: 32
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(32)
 <223> OTHER INFORMATION: Human acceptor E FR3

<400> SEQUENCE: 87

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 1 5 10 15

Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys
 20 25 30

<210> SEQ ID NO 88
 <211> LENGTH: 10
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(10)
 <223> OTHER INFORMATION: Human acceptor E FR4

<400> SEQUENCE: 88

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 1 5 10

<210> SEQ ID NO 89
 <211> LENGTH: 23
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(23)
 <223> OTHER INFORMATION: Human acceptor F FR1

<400> SEQUENCE: 89

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys
 20

<210> SEQ ID NO 90
 <211> LENGTH: 15
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(15)
 <223> OTHER INFORMATION: Human acceptor F FR2

<400> SEQUENCE: 90

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
 1 5 10 15

-continued

<210> SEQ ID NO 91
 <211> LENGTH: 32
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(32)
 <223> OTHER INFORMATION: Human acceptor F FR3

<400> SEQUENCE: 91

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 1 5 10 15
 Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys
 20 25 30

<210> SEQ ID NO 92
 <211> LENGTH: 10
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(10)
 <223> OTHER INFORMATION: Human acceptor F FR4

<400> SEQUENCE: 92

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 1 5 10

<210> SEQ ID NO 93
 <211> LENGTH: 719
 <212> TYPE: PRT
 <213> ORGANISM: Mus musculus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1)..(719)
 <223> OTHER INFORMATION: mCSF1R ECD-Fc

<400> SEQUENCE: 93

Ala Pro Val Ile Glu Pro Ser Gly Pro Glu Leu Val Val Glu Pro Gly
 1 5 10 15
 Glu Thr Val Thr Leu Arg Cys Val Ser Asn Gly Ser Val Glu Trp Asp
 20 25 30
 Gly Pro Ile Ser Pro Tyr Trp Thr Leu Asp Pro Glu Ser Pro Gly Ser
 35 40 45
 Thr Leu Thr Thr Arg Asn Ala Thr Phe Lys Asn Thr Gly Thr Tyr Arg
 50 55 60
 Cys Thr Glu Leu Glu Asp Pro Met Ala Gly Ser Thr Thr Ile His Leu
 65 70 75 80
 Tyr Val Lys Asp Pro Ala His Ser Trp Asn Leu Leu Ala Gln Glu Val
 85 90 95
 Thr Val Val Glu Gly Gln Glu Ala Val Leu Pro Cys Leu Ile Thr Asp
 100 105 110
 Pro Ala Leu Lys Asp Ser Val Ser Leu Met Arg Glu Gly Gly Arg Gln
 115 120 125
 Val Leu Arg Lys Thr Val Tyr Phe Phe Ser Pro Trp Arg Gly Phe Ile
 130 135 140
 Ile Arg Lys Ala Lys Val Leu Asp Ser Asn Thr Tyr Val Cys Lys Thr
 145 150 155 160
 Met Val Asn Gly Arg Glu Ser Thr Ser Thr Gly Ile Trp Leu Lys Val
 165 170 175

Asn	Arg	Val	His	Pro	Glu	Pro	Pro	Gln	Ile	Lys	Leu	Glu	Pro	Ser	Lys
			180				185						190		
Leu	Val	Arg	Ile	Arg	Gly	Glu	Ala	Ala	Gln	Ile	Val	Cys	Ser	Ala	Thr
			195				200						205		
Asn	Ala	Glu	Val	Gly	Phe	Asn	Val	Ile	Leu	Lys	Arg	Gly	Asp	Thr	Lys
			210				215						220		
Leu	Glu	Ile	Pro	Leu	Asn	Ser	Asp	Phe	Gln	Asp	Asn	Tyr	Tyr	Lys	Lys
			225				230						235		
Val	Arg	Ala	Leu	Ser	Leu	Asn	Ala	Val	Asp	Phe	Gln	Asp	Ala	Gly	Ile
			245				250						255		
Tyr	Ser	Cys	Val	Ala	Ser	Asn	Asp	Val	Gly	Thr	Arg	Thr	Ala	Thr	Met
			260				265						270		
Asn	Phe	Gln	Val	Val	Glu	Ser	Ala	Tyr	Leu	Asn	Leu	Thr	Ser	Glu	Gln
			275				280						285		
Ser	Leu	Leu	Gln	Glu	Val	Ser	Val	Gly	Asp	Ser	Leu	Ile	Leu	Thr	Val
			290				295						300		
His	Ala	Asp	Ala	Tyr	Pro	Ser	Ile	Gln	His	Tyr	Asn	Trp	Thr	Tyr	Leu
			305				310						320		
Gly	Pro	Phe	Phe	Glu	Asp	Gln	Arg	Lys	Leu	Glu	Phe	Ile	Thr	Gln	Arg
			325				330						335		
Ala	Ile	Tyr	Arg	Tyr	Thr	Phe	Lys	Leu	Phe	Leu	Asn	Arg	Val	Lys	Ala
			340				345						350		
Ser	Glu	Ala	Gly	Gln	Tyr	Phe	Leu	Met	Ala	Gln	Asn	Lys	Ala	Gly	Trp
			355				360						365		
Asn	Asn	Leu	Thr	Phe	Glu	Leu	Thr	Leu	Arg	Tyr	Pro	Pro	Glu	Val	Ser
			370				375						380		
Val	Thr	Trp	Met	Pro	Val	Asn	Gly	Ser	Asp	Val	Leu	Phe	Cys	Asp	Val
			385				390						400		
Ser	Gly	Tyr	Pro	Gln	Pro	Ser	Val	Thr	Trp	Met	Glu	Cys	Arg	Gly	His
			405				410						415		
Thr	Asp	Arg	Cys	Asp	Glu	Ala	Gln	Ala	Leu	Gln	Val	Trp	Asn	Asp	Thr
			420				425						430		
His	Pro	Glu	Val	Leu	Ser	Gln	Lys	Pro	Phe	Asp	Lys	Val	Ile	Ile	Gln
			435				440						445		
Ser	Gln	Leu	Pro	Ile	Gly	Thr	Leu	Lys	His	Asn	Met	Thr	Tyr	Phe	Cys
			450				455						460		
Lys	Thr	His	Asn	Ser	Val	Gly	Asn	Ser	Ser	Gln	Tyr	Phe	Arg	Ala	Val
			465				470						475		
Ser	Leu	Gly	Gln	Ser	Lys	Gln	Glu	Pro	Lys	Ser	Ser	Asp	Lys	Thr	His
			485				490						495		
Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val
			500				505						510		
Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr
			515				520						525		
Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu
			530				535						540		
Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys
			545				550						555		
Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser
			565				570						575		
Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys
			5												

-continued

595	600	605
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro		
610	615	620
Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu		
625	630	635 640
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn		
	645	650 655
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser		
	660	665 670
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg		
	675	680 685
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu		
	690	695 700
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys		
705	710	715

<210> SEQ ID NO 94
 <211> LENGTH: 327
 <212> TYPE: PRT
 <213> ORGANISM: Artificial sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic: Human IgG4 S241P

<400> SEQUENCE: 94

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15
Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80
Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95
Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
100 105 110
Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140
Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
195 200 205
Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp

-continued

	245		250		255										
Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys
	260							265					270		
Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser
	275						280					285			
Arg	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Glu	Gly	Asn	Val	Phe	Ser
	290					295					300				
Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser
	305				310				315					320	
Leu	Ser	Leu	Ser	Leu	Gly	Lys									
				325											

<210> SEQ ID NO 95
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (1) .. (107)
 <223> OTHER INFORMATION: Human Igk

<400> SEQUENCE: 95

Arg	Thr	Val	Ala	Ala	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu
1			5					10						15	
Gln	Leu	Lys	Ser	Gly	Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe
	20						25						30		
Tyr	Pro	Arg	Glu	Ala	Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln
	35					40					45				
Ser	Gly	Asn	Ser	Gln	Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser
	50				55					60					
Thr	Tyr	Ser	Leu	Ser	Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu
65			70						75					80	
Lys	His	Lys	Val	Tyr	Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser	Ser
			85					90						95	
Pro	Val	Thr	Lys	Ser	Phe	Asn	Arg	Gly	Glu	Cys					
			100				105								

The invention claimed is:

1. An isolated nucleic acid comprising:

- a) a polynucleotide sequence that encodes a heavy chain comprising a heavy chain (HC) complementarity determining factor (CDR) 1 having the sequence of SEQ ID NO: 15, an HC CDR2 having the sequence of SEQ ID NO: 16, and an HC CDR3 having the sequence of SEQ ID NO: 17; or
- b) a polynucleotide sequence that encodes a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 18, a LC CDR2 having the sequence of SEQ ID NO: 19, and a LC CDR3 having the sequence of SEQ ID NO: 20; or
- c) a first polynucleotide sequence that encodes a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 15, an HC CDR2 having the sequence of SEQ ID NO: 16, and an HC CDR3 having the sequence of SEQ ID NO: 17, and a second polynucleotide sequence that encodes a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 18, a LC CDR2 having the sequence of SEQ ID NO: 19, and a LC CDR3 having the sequence of SEQ ID NO: 20.

2. The isolated nucleic acid of claim 1, wherein the heavy chain is humanized, or the light chain is humanized, or both the heavy chain and the light chain are humanized.

3. The isolated nucleic acid of claim 1, comprising:

- a) a polynucleotide sequence that encodes a heavy chain comprising a sequence of SEQ ID NO: 39; or
 - b) a polynucleotide sequence that encodes a light chain comprising a sequence of SEQ ID NO: 46; or
 - c) a first polynucleotide sequence that encodes a heavy chain comprising a sequence of SEQ ID NO: 39 and a second polynucleotide sequence that encodes a light chain comprising a sequence of SEQ ID NO: 46.
4. The isolated nucleic acid of claim 3, comprising:
- a) a polynucleotide sequence that encodes a heavy chain comprising a sequence of SEQ ID NO: 53; or
 - b) a polynucleotide sequence that encodes a light chain comprising a sequence of SEQ ID NO: 60; or
 - c) a first polynucleotide sequence that encodes a heavy chain comprising a sequence of SEQ ID NO: 53 and a second polynucleotide sequence that encodes a light chain comprising a sequence of SEQ ID NO: 60.
5. The isolated nucleic acid of claim 3, comprising:
- a) a polynucleotide sequence that encodes a heavy chain consisting of a sequence of SEQ ID NO: 53; or

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- b) a polynucleotide sequence that encodes a light chain consisting of a sequence of SEQ ID NO: 60; or
 - c) a first polynucleotide sequence that encodes a heavy chain consisting of a sequence of SEQ ID NO: 53 and a second polynucleotide sequence that encodes a light chain consisting of a sequence of SEQ ID NO: 60.
6. An isolated host cell comprising:
- a) a nucleic acid comprising a first polynucleotide sequence that encodes a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 15, an HC CDR2 having the sequence of SEQ ID NO: 16, and an HC CDR3 having the sequence of SEQ ID NO: 17, and a second polynucleotide sequence that encodes a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 18, a LC CDR2 having the sequence of SEQ ID NO: 19, and a LC CDR3 having the sequence of SEQ ID NO: 20; or
 - b) a first nucleic acid comprising a first polynucleotide sequence that encodes a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 15, an HC CDR2 having the sequence of SEQ ID NO: 16, and an HC CDR3 having the sequence of SEQ ID NO: 17, and a second nucleic acid comprising a second polynucleotide sequence that encodes a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 18, a LC CDR2 having the sequence of SEQ ID NO: 19, and a LC CDR3 having the sequence of SEQ ID NO: 20.
7. The host cell of claim 6, wherein the heavy chain and the light chain are humanized.
8. The host cell of claim 6, wherein:
- a) the nucleic acid comprises a first polynucleotide sequence that encodes a heavy chain comprising a sequence of SEQ ID NO: 39 and a second polynucleotide sequence that encodes a light chain comprising a sequence of SEQ ID NO: 46; or
 - b) the first nucleic acid comprises a first polynucleotide sequence that encodes a heavy chain comprising a sequence of SEQ ID NO: 39 and the second nucleic acid comprises a second polynucleotide sequence that encodes a light chain comprising a sequence of SEQ ID NO: 46.
9. The host cell of claim 8, wherein:
- a. the nucleic acid comprises a first polynucleotide sequence that encodes a heavy chain comprising a sequence of SEQ ID NO: 53 and a second polynucleotide sequence that encodes a light chain comprising a sequence of SEQ ID NO: 60; or
 - b. the first nucleic acid comprises a first polynucleotide sequence that encodes a heavy chain comprising a sequence of SEQ ID NO: 53 and the second nucleic acid

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- comprises a second polynucleotide sequence that encodes a light chain comprising a sequence of SEQ ID NO: 60.
10. The host cell of claim 8, wherein:
- a. the nucleic acid comprises a first polynucleotide sequence that encodes a heavy chain consisting of a sequence of SEQ ID NO: 53 and a second polynucleotide sequence that encodes a light chain consisting of a sequence of SEQ ID NO: 60; or
 - b. the first nucleic acid comprises a first polynucleotide sequence that encodes a heavy chain consisting of a sequence of SEQ ID NO: 53 and the second nucleic acid comprises a second polynucleotide sequence that encodes a light chain consisting of a sequence of SEQ ID NO: 60.
11. The host cell of claim 6, which is a CHO cell or a 293 cell.
12. The host cell of claim 7, which is a CHO cell or a 293 cell.
13. The host cell of claim 8, which is a CHO cell or a 293 cell.
14. The host cell of claim 9, which is a CHO cell or a 293 cell.
15. The host cell of claim 10, which is a CHO cell or a 293 cell.
16. A method of producing an antibody that binds colony stimulating factor 1 receptor (CSF1R), comprising culturing the host cell of claim 6 under conditions sufficient to produce the antibody.
17. A method of producing an antibody that binds colony stimulating factor 1 receptor (CSF1R), comprising culturing the host cell of claim 7 under conditions sufficient to produce the antibody.
18. A method of producing an antibody that binds colony stimulating factor 1 receptor (CSF1R), comprising culturing the host cell of claim 8 under conditions sufficient to produce the antibody.
19. A method of producing an antibody that binds colony stimulating factor 1 receptor (CSF1R), comprising culturing the host cell of claim 9 under conditions sufficient to produce the antibody.
20. A method of producing an antibody that binds colony stimulating factor 1 receptor (CSF1R), comprising culturing the host cell of claim 10 under conditions sufficient to produce the antibody.
21. The method of claim 16, wherein the antibody is selected from a Fab, an Fv, an scFv, a Fab', and a (Fab')₂.
22. The method of claim 17, wherein the antibody is selected from a Fab, an Fv, an scFv, a Fab', and a (Fab')₂.
23. The method of claim 18, wherein the antibody is selected from a Fab, an Fv, an scFv, a Fab', and a (Fab')₂.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 9,200,075 B2
APPLICATION NO. : 14/266209
DATED : December 1, 2015
INVENTOR(S) : Justin Wong et al.

Page 1 of 1

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the title page item 57

In the Abstract:

At line 5, "lights" should read --light--.

In the claims

In Claim 1:

At column 159, line 48, "complimentarity" should read --complementarity--.

Signed and Sealed this
Nineteenth Day of April, 2016

A handwritten signature in black ink, reading "Michelle K. Lee". The signature is fluid and cursive, with the first letters of each name being capitalized and prominent.

Michelle K. Lee
Director of the United States Patent and Trademark Office